SANFORD GUIDE®

熱病®

Thirty-fifth Edition

THE SANFORD GUIDE TO ANTIMICROBIAL THERAPY 2005

David N. Gilbert, M.D.
Robert C. Moellering, Jr., M.D.
George M. Eliopoulos, M.D.
Merle A. Sande, M.D.

EDITORS' NOTE

Welcome to the 35th Edition of the SANFORD GUIDE TO ANTIMICROBIAL THERAPY The Editors call your attention to some of the many changes from the 34th Edition

- Gemifloxacin and telithromycin are now FDA-approved and indicated for selected respiratory tract infections
- Rifaximin was approved for traveler's diarrhea Both tinidazole and nitazoxanide have FDA approval for giardiasis Tinidazole is very helpful for metronidazole-resistant trichomonas vaginitis
- Selecting therapy for drug-resistant bacteria is a continuing challenge Recommendations for treatment of community-acquired MRSA and multi-drug resistant Gram-negative bacilli appear in several tables
- A new figure (Figure 1, page 27) provides a treatment algorithm for M tuberculosis
- Table 15D was added to summarize management of patients exposed to HIV and/or viral hepatitis
- All other tables are updated with respect to empiric and specific drug therapy, antimicrobial prophylaxis, and drug-drug interactions, as well as drug doses, costs, and adverse effects

Some of the recommendations in the SANFORD GUIDE suggest use of agents for purposes or in dosages other than recommended in product labeling Such recommendations are based on reports in peer-reviewed publications, they are not based on direct input from any pharmaceutical manufacturer They are made only with due consideration of the concerns of the Food and Drug Administration for "off-label" uses We identify some such uses, but not all, as "not FDA-approved for this indication."

As always, the Editors are deeply indebted to Carolyn Wickwire for her exceptional ability and devotion to preparation of the final manuscript

Last, we welcome input from our readers Your suggestions, inquiries and observations result in annual improvements to the SANFORD GUIDE

David N Gilbert, M D
Robert C Moellering Jr , M D
George M Eliopoulos, M D
Merle A Sande, M D
Editors
January 2005

SANFORD GUIDE®

Thirty-fifth Edition

THE SANFORD GUIDE TO ANTIMICROBIAL THERAPY 2005

David N. Gilbert, M.D.
Director of Medical Education & Earl A. Chiles Research Institute
Providence Portland Medical Center
Professor of Medicine
Oregon Health Sciences University
Portland, Oregon

Robert C. Moellering, Jr., M.D.
Physician-in-Chief, Beth Israel Deaconess Medical Center
Herman L. Blumgart Professor of Medicine
Harvard Medical School
Boston, Massachusetts

George M. Eliopoulos, M.D.
Chief, James L. Tullis Firm, Beth Israel Deaconess Hospital
Professor of Medicine
Harvard Medical School
Boston, Massachusetts

Merle A. Sande, M.D.
Clarence M. & Ruth N. Birrer Professor of Medicine
University of Utah School of Medicine
Salt Lake City, Utah

THE SANFORD GUIDE TO ANTIMICROBIAL THERAPY 2005
35TH EDITION

Jay P. Sanford, M.D.
1928-1996

Editors

David N. Gilbert, M.D.
George M. Eliopoulos, M.D.
Robert C. Moellering, Jr., M.D.
Merle A. Sande, M.D.

The Sanford Guides are published annually by

ANTIMICROBIAL THERAPY, INC.
PO Box 70, 229 Main Street, Hyde Park, VT 05655 USA
Tel 802-888-2855 Fax 802-888-2874
Email info@sanfordguide.com www.sanfordguide.com

Printed in the United States of America
ISBN 978-1-930808-22-4
Pocket Edition (English)

PUBLISHER'S PREFACE

This edition marks the 35th revision of the SANFORD GUIDE TO ANTIMICROBIAL THERAPY. The genesis of the SANFORD GUIDE was a grand rounds lecture by Jay P. Sanford on new antibiotics (amoxicillin). The lecture handout was a table, organized by anatomic site, summarizing etiologies, suggested regimens and comments on therapy. This handout became, and remains, the core of the SANFORD GUIDE -- Table 1 --Initial Choice of Antimicrobial Therapy. As the issues in treatment of infectious diseases have grown in number and complexity, the SANFORD GUIDE has evolved and expanded. Yet it remains consistent with Jay P. Sanford's vision: to provide the professional with a handy, up-to-date reference tool to assist in making informed clinical decisions.

Though many readers of the SANFORD GUIDE receive their copy from a pharmaceutical company representative, please be assured that the SANFORD GUIDE has been, and continues to be, independently prepared and published since its inception in 1969. Decisions regarding the content of the SANFORD GUIDE are solely those of the editors and the publisher. We welcome your questions, comments and feedback concerning the SANFORD GUIDE. All of your feedback is reviewed and taken into account in preparing the next edition.

NOTE TO READER

Every effort is made to ensure the accuracy of the content of this guide. However, current full prescribing information available in the package insert of each drug should be consulted before prescribing any product. The editors and publisher are not responsible for errors or omissions or for any consequences from application of the information in this book and make no warranty, express or implied, with respect to the currency, accuracy, or completeness of the contents of the publication. Application of this information in a particular situation remains the professional responsibility of the practitioner.

—TABLE OF CONTENTS —

TABLE 1
CLINICAL APPROACH TO INITIAL CHOICE OF ANTIMICROBIAL THERAPY
Treatment based on presumed site or type of infection. In selected instances, treatment and prophylaxis based on identification of pathogens

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[‡]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
ABDOMEN: *See Peritoneum, page 31, Gallbladder, page 10, and Pelvic Inflammatory Disease, page 16*				
BONE: Osteomyelitis. Microbiologic diagnosis is essential. If blood culture negative, need culture of bone. Culture of sinus tract drainage not predictive of bone culture. Review *Ln 364: 369, 2004*				
Hematogenous Osteomyelitis				
Empiric therapy—Collect bone and blood cultures before empiric therapy				
Newborn (<4 mos.) *See Table 16 for dose*	S. aureus, Gm-neg. bacilli, Group B strep	**MRSA possible: Vanco** + **P. Ceph 3**	**MRSA unlikely:** (**Nafcillin** or **oxacillin**) + **P. Ceph 3**	*Table 16 for dose.* Severe allergy or toxicity: (Linezolid[NAI] 10 mg/kg IV/po q8h + aztreonam). Could substitute clindamycin for linezolid
Children (>4 mos.)	S. aureus, Group A strep, Gm-neg. bacilli rare	**MRSA possible: Vanco**	**MRSA unlikely: Nafcillin** or **oxacillin**	Severe allergy or toxicity: Clinda or TMP/SMX or linezolid[NAI]. *Dosages in Table 16*
		Add **P. Ceph 3** if Gm-neg. bacilli on Gram stain. *Doses, Table 16*		
Adult (>21 yrs.) **Vertebral osteo ± epidural abscess**, other sites	S. aureus most common but variety other organisms. **Blood & bone cultures essential.**	**MRSA possible: Vanco** 1.0 gm IV q12h	**MRSA unlikely: Nafcillin** or **oxacillin** 2.0 gm IV q4h	**Dx: MRI early to look for epidural abscess.** Allergy or toxicity: TMP/SMX 8–10 mg/kg/d div. q8h IV or linezolid 600 mg IV/po q12h (*AnIM 138: 135, 2003*)[NAI]
Specific therapy—Culture and in vitro susceptibility results known				
	MSSA	**Nafcillin** or **oxacillin** 2.0 gm q4h IV or **cefazolin** 2.0 gm q8h IV	**Vanco** 1.0 gm q12h IV	Severe allergy or toxicity: Clinda 600–900 mg IV q8h or TMP/SMX 8–10 mg/kg/d div. q8h IV. **If no response to clinda, check for "inducible" resistance.** If susceptible in vitro: (CIP 750 mg po bid or Levo 750 mg po 1x/d.) + RIF 300 mg po bid.
	MRSA—*See Table 4, page 51, Resistant bacteria*	**Vanco** 1.0 gm q12h IV	**Linezolid** 600 mg q12h IV/po	Severe allergy or toxicity: Clinda 600–900 mg q8h IV (check for inducible/ constitutive resistance), TMP/SMX 8–10 mg/kg/d div. q8h IV. No data for daptomycin. *See Table 4, page 51, Resistant bacteria*
Hemoglobinopathy: Sickle cell/thalassemia	Salmonella, other Gm-neg. bacilli	**CIP** 400 mg IV q12h	**Levo** 750 mg IV q24h	Thalassamia: transfusion and iron chelation risk factors
Contiguous Osteomyelitis Without Vascular Insufficiency				
Empiric therapy: Get cultures!				
Foot bone: osteo due to nail through tennis shoe	P. aeruginosa	**CIP** 750 mg bid po or **Levo** 750 mg q24h po	**Ceftaz** 2.0 gm q8h IV or **CFP** 2.0 gm q12h IV	*See Skin—Nail puncture, page 38.* Need debridement to remove foreign body
Long bone post-internal fixation of fracture	S. aureus, Gm-neg. bacilli, P. aeruginosa	**Vanco** 1.0 gm q12h IV + [**ceftaz** or **CFP** (*see footnote*[†])] *See Comment*	**Linezolid** 600 mg IV/po bid[NAI] + (**ceftaz** or **CFP**) *See Comment*	Often necessary to remove hardware to allow bone union. May need revascularization. Regimens listed are empiric. Adjust after culture data available. If susceptible Gm-neg. bacillus: CIP 750 mg po bid or Levo 750 mg po 1x/d
Prosthetic joint	*See Prosthetic joint, page 22*			
Sternum, post-op	S. aureus, S. epidermidis	**Vanco** 1.0 gm q12h IV	**Linezolid** 600 mg bid po/IV[NAI]	Sternal debridement for cultures & removal of necrotic bone
Contiguous Osteomyelitis With Vascular Insufficiency Ref: *CID S115–22, 2004*				
Most pts are **diabetics** with peripheral neuropathy & infected skin ulcers (*see Diabetic foot, page 10*)	Polymicrobic [Gm+ cocci (to include MRSA) (aerobic & anaerobic) and Gm-neg. bacilli (aerobic & anaerobic)]	Ideally, debride overlying ulcer & submit bone for histology & culture. Revascularize if possible. Full contact cast. Specific antibiotic(s) x6 wks		**Diagnosis of osteo:** Culture of biopsied bone gold standard. Marrow edema on MRI best imaging. Probe to bone has high predictive value. **Treatment:** (1) Revascularize if possible. (2) Culture bone. (3) Specific antimicrobial(s). (4) Full contact cast

[†] Drug dosage: **IMP** 0.5 gm q6h IV. **MER** 1.0 gm q8h IV (not licensed indication but should be effective). **ERTA** 1.0 gm q24h. **TC/CL** 3.1 gm q6h IV. **PIP/TZ** 3.375 gm q6h or 4.5 gm q8h IV. **AM/SB** 3.0 gm IV q6h. **ceftazidime** 2.0 gm q8h IV. **CFP** 2.0 gm q12h IV. **metro** 1.0 gm loading dose and then 0.5 gm q6h IV or po or 1.0 gm q12h IV. **aztreonam** 2.0 gm q8h IV. **vanco** 1.0 gm q12h IV.

(Footnotes and abbreviations on page 45)

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. **NAI** = *Not FDA approved indication*

TABLE 1 (2)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
BONE *(continued)*				
Chronic Osteomyelitis: Specific therapy By definition implies presence of dead bone **Need valid cultures**	S aureus Enterobacteriaceae P aeruginosa	**Empiric rx not indicated.** Base systemic rx on results of culture sensitivity testing If acute exacerbation of chronic osteo rx as acute hematogenous osteo		Important adjuncts removal of orthopedic hardware surgical debridement vascularized muscle flaps distraction osteogenesis (Ilizarov) techniques Antibiotic-impregnated cement & hyperbaric oxygen adjunctive NOTE RIF + (vanco or β-lactam) effective in animal model and in a clinical trial of S aureus chronic osteo *(SMJ 79 947, 1986)*
BREAST: Mastitis—Obtain culture, need to know if MRSA present				
Postpartum mastitis				
Mastitis without abscess Ref *JAMA 289 1609, 2003*	S aureus less often S pyogenes (Gp A or B) E coli bacteroides species maybe Corynebacterium sp & selected coagulase-neg staphylococci	**NO MRSA: Outpatient: Dicloxacillin** 500 mg qid po or **cefalexin** 500 mg qid po **Inpatient: Nafcillin/oxacillin** 2 0 gm q4h IV	**MRSA Possible: Outpatient: TMP/SMX-DS** bid po **Inpatient: Vanco** 1 0 gm q12h IV	If no abscess, increased frequency of nursing may hasten response, no risk to infant Corynebacterium sp assoc with chronic granulomatous mastitis *(CID 35 1434, 2002)*
Mastitis with abscess				With abscess, d/c nursing I&D standard needle aspiration reported successful *(Am J Surg 182 117, 2001)* Resume breast feeding from affected breast as soon as pain allows
Non-puerperal mastitis with abscess	S aureus less often Bacteroides sp peptostreptococcus & selected coagulase-neg staphylococci			**If subareolar & odoriferous** most likely anaerobes need to **add metro** 500 mg IV or po tid If not subareolar staph Need pretreatment aerobic/anaerobic cultures Surgical drainage for abscess
CENTRAL NERVOUS SYSTEM				
Brain abscess				
Primary or contiguous source *Ref CID 25 763, 1997*	Streptococci (60–70%) bacteroides (20–40%) Enterobacteriaceae (25–33%) S aureus (10–15%) Rare Nocardia *(Table 11A, page 80)*	**P Ceph 3 (cefotaxime** 2 0 gm q4h IV or **ceftriaxone** 2 0 gm q12h IV) + **metro** 7 5 mg/kg q6h or 15 mg/kg q12h IV	**Pen G** 20–24 mU IV qd + **metro** 7 5 mg/kg q6h or 15 mg/kg q12h IV	If CT scan suggests cerebritis *(JNS 59 972, 1983)* abscesses <2 5 cm and pt neurologically stable and conscious start antibiotics and observe Otherwise, surgical drainage necessary Neurologic deterioration usually mandates surgery Experience with Pen G (HD) + metro without P Ceph 3 or nafcillin/oxacillin has been good We use P Ceph 3 because of frequency of isolation of Enterobacteriaceae **S. aureus rare without positive blood culture; if S. aureus, include vanco until susceptibility known** Strep milleri group esp prone to produce abscess
		Duration of rx unclear rx until response by neuroimaging (CT/MRI)		
Post-surgical, post-traumatic	S aureus, Enterobacteriaceae	(**Nafcillin** or **oxacillin**) 2 0 gm q4h IV + **P Ceph 3**	**Vanco** 1 0 gm q12h IV + **P Ceph 3**	**If MRSA a consideration, substitute vanco for nafcillin or oxacillin.** P Ceph 3 dose as for brain abscess
HIV-1 infected (AIDS)	Toxoplasma gondii	*See Table 13, page 97*		
Subdural empyema In adult 60–90% are extension of sinusitis or otitis media Rx same as primary brain abscess Surgical emergency must drain *(CID 20 372, 1995)*				
Encephalitis/encephelopathy Ref *Ln 359 507, 2002* *(See Table 14, page 108 and for rabies, Table 20C page 141)*	Herpes simplex arboviruses rabies West Nile virus Rarely listeria cat-scratch disease	Start IV **acyclovir** while awaiting results of CSF PCR for H simplex		Newly recognized strain of bat rabies May not require a break in the skin Eastern equine encephalitis causes focal MRI changes in basal ganglia and thalamus *(NEJM 336 1867, 1997)* Cat-scratch rat *PIDJ 14 866, 1995)* Ref on West Nile & related viruses *NEJM 351 370, 2004*
Meningitis, "Aseptic": Pleocytosis of 100s of cells CSF glucose normal, neg culture for bacteria *(see Table 14, page 104)*	Enteroviruses HSV-2, LCM HIV, other viruses drugs (NSAIDs metronidazole carbamazepine, TMP/SMX IVIG) rarely leptospirosis	For all but leptospirosis, IV fluids and analgesics D/C drugs that may be etiologic For lepto (**doxy** 100 mg q12h IV or po) or (**Pen G** 5 mU q6h IV) or (**AMP** 0 5–1 0 gm q6h IV) Repeat LP if suspect partially-treated bacterial meningitis		If available, PCR of CSF for enterovirus HSV-2 unusual without concomitant genital herpes Drug-induced aseptic meningitis *ArIM 159 1185, 1999* For lepto positive epidemiologic history and concomitant hepatitis, conjunctivitis dermatitis, nephritis

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (3)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (uaual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[4]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
CENTRAL NERVOUS SYSTEM *(continued)*				
Meningitia, Bacteriel, Acute: Goal ia empiric therapy, than CSF exam within 30 min. If focal neurologic deficit, giva empiric rx, then do head CT, then do LP. *(CID 39 1267, 2004)* NOTE In children treatment caused CSF cultures to turn neg in 2 hrs with meningococci & partial response with pneumococci in 4 hrs *(Peds 108 1169, 2001)*				
Empiric Therapy—CSF Gram atain ia negative—immunocompatent				
Age Preterm to <1 month *Ln 361 2139 2003*	Group B strep 49%, E coli 18% listeria 7% misc Gm-neg 10% misc Gm-pos 10%	**AMP + cefotaxima** Intraventricular rx not recommended Repeat CSF exam/culture 24–36 hrs after start of rx *For dosage see Table 16*	**AMP + gentamicin**	Primary & alternative regimens active vs Group B strep most coliforms & listeria If premature infant with long nursery stay S aureus enterococci and resistant coliforms potential pathogens Optional empiric regimens [nafcillin + (ceftazidime or cefotaxime)] If high risk of MRSA use vanco + cefotaxime Alter regimen after culture/sensitivity data available
Age: 1 mo.– 50 yrs 1999–2000 respiratory disease season 34 1% of S pneumo in U S were either intermediate in susceptibility or resistant to concentrations of Pen G achieved in CSF [*CID 34 (Suppl 1) S4 2002*] **See footnote[1]** for empiric treatment rationale	S pneumo meningococci H influenzae now very rare **listeria unlikely if young & immunocompetent**	Adult dosage [(**Cefotaxime** 2 0 gm q4–6h IV OR **ceftriaxone** 2 gm IV q12h)] + (**dexemethaasone**) + **vanco** *(see footnote[2])* Peds *see footnote[3]*	[(**MER** 2 0 gm q8h IV) (Peds 40 mg/kg IV q8h)] + IV **dexamethasone** + **vanco** *(see footnote[2])* Peds *see footnote[3]*	**For pts with aevera pen. allergy: Chloro** 50 mg/kg/d IV div q6h (max 4 gm/d) (for meningococcus) + **TMP/SMX** 15–20 mg/kg/d div q6–8h (for listeria if immunocompromised) + **vanco** Rare meningococcal isolates chloro-resistant *(NEJM 339 868 1998)* The standard alternative for pts with severe pen allergy was chloro However high failure rate in pts with DRSP *(Ln 339 405, 1992, Ln 342 240 1993)* **So far, no vanco-raelatant S. pneumo.** **Value of dexamethasone** documented in children with H influenzae & now confirmed in adults with S pneumo & N meningitidis *(NEJM 347 1549 & 1613 2002 UnID 4 139 2004)* **Give 1[st] dose 15–20 min. Prior to or concomitant with 1[st] dose of antibiotic. Dosa: 0.15 mg/kg IV q6h x2–4 d.** **For meningococcal immunization, aea *Tabla 20, pegaa 139–140.***
		Oexamathaaone 0 15 mg/kg IV q6h x2–4 d **Give with or just before 1[st] dosa of antibiotic to block TNF production *(aee Comment).*** *See footnote regarding drug resistant S pneumo[1]* *See footnote[3] for rest of ped dosage*		
Age: >50 yrs or alcoholism or other **debilitating aaaociated diaeaaes** or **impaired cellular immunity**	S pneumo listeria Gm-neg bacilli Note absence of meningococcus	(**AMP** 2 0 gm IV q4h) + (**ceftriaxona** 2 0 gm IV q12h or **cefotaxime** 2 0 gm IV q6h) + **vanco** + IV **dexamethasona** For vanco dose see footnote[2] **Daxamethasone** 0 15 mg/kg q6h IV x2–4 d 1[st] dose before or concomitant with 1[st] dose of antibiotic	**MER** 2 0 gm q8h IV + **vanco** + IV **dexamethasone** ***For severe pen. Allergy, aea Comment***	**Severe penicillin allergy: Vanco** 500–750 mg q6h IV + **TMP/SMX** 15–20 mg/kg/d div q6–8h pending culture results Chloro has failed vs DRSP *(Ln 342 240 1993)* MER active vs listeria in vitro *[JAC 36(Suppl A) 1 1995]* CSF levels appear adequate *(JAC 34 175 1994)* but no clinical data *(PIDJ 18 581 1999)*
Post-neurosurgery, post-head trauma, or post-cochlaar implant *(NEJM 349 435, 2003)*	S pneumoniae most common esp if CSF leak Other S aureus, coliforms P aeruginosa	**Vanco** (until known not MRSA) 500–750 mg q6h[2] IV + (**cefepima** or **ceftazidime** 2 0 gm q8h IV) *(see Comment)*	**MER** 2 0 gm q8h IV + **vanco** 1 0 gm q6–12h IV	**Vanco** alone not optimal for S pneumo If/when suscept S pneumo identified quickly switch to **ceftriaxone** or **cefotaxime** If coliform or pseudomonas meningitis some add intrathecal gentamicin (4 mg q12h into lateral ventricles) Cure of acinetobacter meningitis with intrathecal colistin *(JAC 53 290, 2004)*
Ventriculitis/meningitie due to infected ventriculo-peritoneal (atrial) ahunt	S epidermidis S aureus coliforms diphtheroids (rare) P acnes	**Vanco** 500–750 mg q6h IV + (**cefepima** or **ceftazidime** 2 0 gm q8h IV)	**Vanco** 500–750 mg q6h IV + **MER** 2 0 gm q8h IV	Usual care 1[st] remove infected shunt & culture external ventricular catheter for drainage/pressure control antimicrobic x10–14 d For timing of new shunt see *CID 39 1267 2004*

[1] **Rationala** Hard to get adequate CSF concentrations of anti-infectives hence MIC criteria for in vitro susceptibility are lower for CSF isolates *(ArIM 161 2538 2001)*

[2] Low and erratic penetration of **vanco** into the CSF *(PIDJ 16 895 1997)* Recommended **dosaga in children** is 15 mg/kg q6h IV (double the standard adult dose) **In adults,** a maximum dose of 2 3 gm/day is suggested **500–750 mg q6h IV**

[3] **Oaaage of druga uaed to rx children ≥1 mo. of aga:** Cefotaxime 200 mg/kg/d IV div q6–8h ceftriaxone 100 mg/kg/d IV div q12h vanco 15 mg/kg IV q6h

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (4)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
CENTRAL NERVOUS SYSTEM *(continued)*				
Meningitis, Bacterial, Acute *(continued) (CID 39 1267 2004)*				
Empiric Therapy—Positive CSF Gram stain				
Gram-positive diplococci	S pneumoniae	Either (**ceftriexone** 2 0 gm IV q12h or **cafotaxima** 2 0 gm IV q4–6h) + **vanco** 500–750 mg IV q6h + timed **daxamethasona** 0 15 mg/kg q6h IV x2–4 d	**Alternatives: MER** 2 0 gm IV q8h or **Moxi** 400 mg IV once daily or **Gati** 400 mg IV once daily All + **dexamathasone**	
Gram negative diplococci	N meningitidis	(**Cefotaxime** 2 0 gm IV q4–6h or **caftriaxone** 2 0 gm IV q12h) + timed **dexamathasone** *(dose above)*	**Alternativas: Pen G** 4 mill units IV q4h or **AMP** 2 0 gm q4h or **Gatl/Moxl** 400 mg IV once daily or **chloro** 1 0 gm IV q6h	
Gram-positive bacilli or coccobacilli	Listeria monocytogenes	**AMP** 2 0 gm IV q4h ± **gantamicin** 2 mg/kg loading dose then 1 7 mg/kg q8h	Listeria ret *CID 24 1 1997* **If pan.-allergic, use TMP/SMX 15–20 mg/kg/d. div q6–8h or MER 2.0 gm IV q8h**	
Gram-negative bacilli	H influenzae coliforms P aeruginosa	(**Ceftazidime** or **cefepime** 2 0 gm IV q8h) + **gentamicin** 2 mg/kg 1st dose then 1 7 mg/kg q8h	**Alternatives: CIP** 400 mg IV q8–12h **MER** 2 0 gm IV q8h	
Specific Therapy—Positive cultura of CSF with in vitro auaceptibility results availeble. Interest in monitoring/reducing intracranial pressure *CID 38 384 2004*				
H influenzae	β lactamase +	**Ceftriaxone** (peds) 100 mg/kg/d IV div q12h	**Pen. allargic: Chloro** 50 mg/kg/d IV div q6h (max 4 gm/d)	
Listeria monocytogenes		**AMP** 2 0 gm IV q4h ± **gentamicin** 2 mg/kg loading dose then 1 7 mg/kg q8h	**Pen. allergic: TMP/SMX** 20 mg/kg/d div q6–12h One report of greater efficacy of AMP + TMP/SMX as compared to AMP + gentamicin *(JID 33 79 1996)* **Alternativa: MER** 2 0 gm IV q8h	
N meningitidis	MIC 0 1–1 0 µg/ml	**Ceftriaxone** 2 0 gm IV q12h x7 d *(see Comment)* if pen allergic **chloro** 50 mg/kg (up to 1 0 gm) IV q6h	Rare isolates chloro-resistant *(NEJM 339 368 & 917 1998)* **Alternatives. MER** 2 0 gm IV q8h or **Gatl/Moxl** 400 mg once daily	
S. pneumoniae	Pen G MIC	**Pen G** 4 mU IV q4h or **AMP** 2 0 gm IV q4h	**Alternetives: Ceftriaxone** 2 0 gm IV q12h **chloro** 1 0 gm IV q6h	
NOTES: 1 Assumes dexametha-sone just prior to 1st dose & x4 d 2 If MIC ≥1 0 repeat CSF exam after 24–48h 3 Treat for 10–14 days	<0 1 µg/ml			
	0 1–1 0 µg/ml	**Ceftriaxona** 2 0 gm IV q12h or **cefotaxime** 2 0 gm IV q4–6h	**Alternativas: Cefapime** 2 0 gm IV q8h or **MER** 2 0 gm IV q8h	
	≥2 0 µg/ml	**Vanco** 500–750 mg IV q6h + (**caftriaxone** or **cafotax-ime** as above)	**Alternatives: Gati or Moxl** 400 mg IV once daily	
	Ceftriaxone MIC ≥1 0 µg/ml	**Vanco** 500–750 mg IV q6h + (**ceftriaxona** or **cafotax-ime** as above)	**Alternativas: Gati or Moxi** 400 mg IV once daily	
E coli other coliforms or P aeruginosa	Consultation advised—need susceptibility results	(**Ceftazidime** or **cefepime** 2 0 gm IV q8h) ± **gentamicin**	**Alternatives: CIP** 400 mg IV q8–12h **MER** 2 0 gm IV q8h For discussion of intraventricular thera... *CID 39 1267 2004*	
Prophylexia for H. influenzaa and N. meningitidis				
Hemophilua influenzae type b Household and/or day care contact residing with index case or ≥4 hrs Day care contact same day care as index case for 5–7 days before onset		**RIF** 20 mg/kg po (not to exceed 600 mg) qd x4 doses	**Household:** If there is one unvaccinated contact ≤4 yrs in the household RIF recommended for all household contacts except pregnant women **Child Care Facilities:** With 1 case if attended by unvaccinated children ≤2 yrs consider prophylaxis + vaccinate susceptibles If all contacts >2 yrs no prophylaxis If ≥2 cases in 60 days & unvaccinated children attend prophylaxis recommended for children & personnel *(Am Acad Ped Red Book 1997 page 222)*	

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal funct...

TABLE 1 (5)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE‡	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
CENTRAL NERVOUS SYSTEM/Meningitis, Bacterial/Prophylaxis *(continued)*				
Neisseria meningitidis exposure (close contact) *[MMWR 46(RR-5) 1 1997]* CDC recommends informing college freshmen living in dormitories & residence halls of available vaccine *[MMWR 46(RR-7) 1, 2000 & 50/23 487, 2001]*		[**RIF** 600 mg po q12h x4 doses (Children >1 mo age 10 mg/kg po q12h x4 doses, <1 mo age 5 mg/kg q12h x4 doses)] or [**CIP** (adults) 500 mg po single dose] or [**Ceftriaxone** 250 mg IM x1 dose (child <15 yrs 125 mg IM x1)]		N meningitidis spread by respiratory droplets not aerosols hence close contact required ↑ risk if close contact for at least 4 hrs during week before illness onset (e g , housemates day care contacts cellmates) or exposure to pt s naso-pharyngeal secretions (e g via kissing, mouth-to-mouth resuscitation intubation nasotracheal suctioning) Azithro 500 mg x1 as effective as RIF 600 mg bid x2 d *(PIDJ 17 816, 1998)* Ceftriaxone equivalent to RIF *(JAC 45 909, 2000)*
		Spiramycin 500 mg po q6h x5 d Children 10 mg/kg po q6h x5 d		Primary prophylactic regimen in many European countries
Meningitis, chronic Defined as symptoms + CSF pleocytosis for ≥4 wks	M tbc 40% cryptococcosis 7% neoplastic 8% Lyme syphilis Whipple s disease	Treatment depends on etiology No urgent need for empiric therapy		Long list of possibilities bacteria parasites fungi viruses neoplasms, vasculitis and other miscellaneous etiologies—*see chapter on chronic meningitis in latest edition of Harrison's Textbook of Internal Medicine*
Meningitis, eosinophilic *AJM 114 217 2003* *[See Table 13A, page 98]*	Angiostrongyliasis gnatho stomiasis rarely others	Corticosteroids	Not sure antihelminthic rx works	1/3 lack peripheral eosinophilia Need serology to confirm dx Steroid ret *CID 31 660, 2001* Recent outbreak *NEJM 346 668, 2002*
Meningitis, HIV-1 infected (AIDS)	As in adults >50 yrs also consider cryptococci M tuberculosis syphilis HIV aseptic meningitis Listeria monocytogenes	If etiology not identified rx as adult >50 yrs + obtain CSF/serum cryptococcal antigen *(see Comments)*	For crypto rx *see Table 11A, page 78*	C neoformans most common etiology in AIDS pt H influenzae pneumococci Tbc syphilis viral histoplasma & coccidioides also need to be considered Obtain blood cultures L monocytogenes risk >60x ↑, ¾ present as meningitis *(CID 17 224, 1993)*
EAR				
External otitis				
"Swimmer s ear" *PIDJ 22 299 2003*	Pseudomonas sp Entero-bacteriaceae, Proteus sp (Fungi rare) Acute infection usually 2° S aureus	Eardrops **Oflox 0.3% soln bid** or [(**polymyxin B** + **neomycin** + **hydrocortisone**) qid] or (**CIP** + **hydrocortisone bid**) For acute disease **dicloxacillin** 500 mg po 4x/d		Rx should include gentle cleaning Recurrences prevented (or decreased) by drying with alcohol drops (1/3 white vinegar 2/3 rubbing alcohol) after swimming then antibiotic drops or 2% acetic acid solution Ointments should not be used in ear Do not use neomycin if tympanic membrane punctured
Chronic	Usually 2° to seborrhea	Eardrops [(**polymyxin B** + **neomycin** + **hydrocortisone** qid) + **selenium sulfide**]		Control seborrhea with dandruff shampoo containing selenium sulfide (Selsun) or [(ketoconazole shampoo) + (medium potency steroid solution triamcinolone 0 1%)]
"Malignant otitis externa" Risk groups Diabetes mellitus, AIDS chemotherapy	Pseudomonas aeruginosa in >90%	(**IMP** 0 5 gm q6h IV) or (**MER** 1 0 gm q8h IV) or [**CIP** 400 mg q12h IV (or 750 mg q12h po)] or (**ceftaz** 2 0 gm q8h IV) or (**CFP** 2 gm q12h) or (**PIP** 4–6 gm q4–6h IV + **tobra**) or (**TC** 3 0 gm q4h IV + **tobra**)		CIP po especially useful for outpatient rx with early disease Surgical debridement usually required, but not radical excision R/O osteomyelitis CT or MRI scan more sensitive than x-ray If bone involved rx for 4–6 wks Ref *LnID 4 34, 2004*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (6)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
EAR *(continued)*				
Otitis media—infants, children, adults				
Acute *(NEJM 347 1169, 2002 Pediatrics 113 1451 2004)* For correlation of bacterial eradication from middle ear & clinical outcome *see LnID 2 593 2002*				
Initial empiric therapy of acute otitis media (AOM) **NOTE:** Pending new data **rx children <2 yrs old** If >2 yrs old afebrile no ear pain neg /questionable exam—consider analgesic treatment without anti microbials	Overall detection in middle ear fluid No pathogen 25% Virus 5–48% Bact + virus 15% Bacteria only 55% Role of viruses *Clin Micro Rev 16 230 2003*	**If NO antibiotics in prior month:** **Amox** po HD[1]	**Received antibiotics in prior month:** **Amox** HD[1] or **AM/CL** HD[1] or **cefdinir** or **cefpodoxime** or **cefprozil** or **cefuroxime axetil**	**If allergic to β-lactam drugs ?** If history unclear or rash oral ceph OK avoid ceph if IgE-mediated allergy e g anaphylaxis High failure rate with **TMP/SMX** if etiology is DRSP or H influenzae *(PIDJ 20 260 2001)* **azithro x5 d. or clarithro x10 d.** (both have ↓ activity vs DRSP) **Up to 50% S. pneumo resistant to macrolides** AM/CL superior to azithro in recent controlled trial *(ICAAC Abst 2324 2003)* **Spontaneous resolution:** 90% pts infected with M catarrhalis 50% with H intluenzae and 10% with S pneumoniae overall 80% resolve within 2–14 d *(NEJM 363 465 2004)* Risk of DRSP ↑ with age <2 yrs, antibiotics last 3 mos , and/or daycare affendance Selection of drug based on (1) effectiveness against β-lactamase producing H influenzae & M catarrhalis and (2) effectiveness against S pneumo including DRSP **Cefaclor, loracarbef, & ceftibuten less active vs DRSP** than other agents listed Variable acceptance of drug taste/smell by children 4–8 y o *[PIDJ 19 (Suppl 2) S174, 2000]*
		For dosage, *see footnotes[1] and [2]* **All doses are pediatric** **Duration of rx:** <2 yrs old x10 d ≥2 yrs old x5–7 d Appropriate duration unclear 5 d may be inadequate for severe disease *(NEJM 347 1169, 2002)* **For adult doseges, see *Sinusitis, pegs 33, and Table 10***		
Treatment for clinical failure after 3 days rx	Drug-resistant S pneumoniae main concern	**NO antibiotics in month prior to last 3 days:** **AM/CL** HD[1] or **cefdinir** or **cefpodoxime** or **cefprozil** or **cefuroxime axetil** or IM **ceftriaxone** x3 d	**Antibiotics in month prior to last 3 days:** [(IM **ceftriaxone**) or (**clindamycin**) and/or tympanocentesis] *See clindamycin Comments*	**Clindamycin** not active vs H intluenzae or M catarrhalis S pneumo resistant to macrolides are usually also resistant to clinda Definition of failure no change in ear pain fever bulging TM or otorrhea after 3 days of rx Tympanocentesis will allow culture **Newer FQs activs vs DRSP, but not approved for uss in children** *(PIDJ 23 390 2004)*. **Vanco is active vs DRSP.** Ceftriaxone IM x3 d superior to 1 d treatment vs DRSP *(PIDJ 19 1040 2000)* AM/CL HD reported successful for pen-resistant S pneumo AOM *(PIDJ 20 829, 2001)*
		For dosage *see footnotes[1] and [2]* **All doses are pediatric** Duration of rx as above		
After >48 hre of nasotracheal intubation	Pseudomonas sp klebsiella enterobacter	**Ceftazidime** or **CFP** or **IMP** or **MER** or **TC/CL** or **CIP** *(For dosages, see Ear, malignant otitis externa page 6)*		With nasotracheal intubation >48 hrs about ½ pts will have otitis media with effusion
Prophylaxis: acute otitis media *NEJM 344 403, 2001, PIDJ 22 10, 2003*	Pneumococci H intluenzae M catarrhalis Staph aureus Group A strep **(see Comments)**	**Sulfieoxazole** 50 mg/kg po at bedtime or **emoxicillin** 20 mg/kg po qd	**Use of antibiotics to prevent otitis media is a major contributor to emergence of antibiotic-resistant S. pneumoI** Pneumococcal protein conjugate vaccine decreases freq AOM in general & due to vaccine serotypes Adenoidectomy at time of tympanostomy tubes ↓ need for future hospitalization for AOM *(NEJM 344 1188, 2001)*	

[1] **Amoxicillin UD or HD** = aMoxicillin usual dose or high dose **AM/CL HD** = aMoxicillin/clavulanate high dose **Ooseges in footnote 2.** Data supporting aMoxicillin HD *PIDJ 22 405 2003*

[2] **Drugs and peds dosege (all po unless specified) for acute otitis media: Amoxicillin UD** = 40 mg/kg/d div q12h or q8h **Amoxicillin HD** = 90 mg/kg/d div q12h or q8h **AM/CL HO** = 90 mg/kg/d of amox component **Extra-strength AM/CL oral suspension** (Augmentin ES-600) available with 600 mg AM & 42 9 mg CL per 5 ml—dose 90/6 4 mg/kg/d div bid **Cefuroxime axetil** 30 mg/kg/d div q12h **Ceftriaxone** 50 mg/kg IM x3 d **Clindamycin** 20–30 mg/kg/d div qid (may be effective vs DRSP but no activity vs H influenzae) **Other drugs suitable for drug (e.g., penicillin)-sensitive S. pneumo: TMP/SMX** 8 mg/kg/d of TMP div q12h **Erythro-sulfisoxazole** 50 mg/kg/d of erythro div q6–8h **Clarithro** 15 mg/kg/d div q12h **azithro** 10 mg/kg/d x1 and then 5 mg/kg qd on days 2–5 Other FDA-approved regimens 10 mg/kg qd x3 d & 30 mg/kg x1 **Cefprozil** 30 mg/kg div q12h **cefpodoxime proxetil** 10 mg/kg/d as single dose **cefaclor** 40 mg/kg/d div q8h **loracarbef** 30 mg/kg/d div q12h **Cefdinir** 7 mg/kg q12h or 14 mg/kg q24h

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (7)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
EAR *(continued)*				
Mastoiditis				
Acute				
Outpatient	Strep pneumoniae 22% S pyogenes 16% Staph aureus 7% H influenzae 4% P aeruginosa 4%, others <1%	Empirically same as Acute otitis media above need **vanco** or **nafcillin/oxacillin** if culture + for S aureus		Has become a rare entity presumably as result of the aggressive rx of acute otitis media
Hospitalized		**Cefotaxime** 1–2 gm IV q4–8h (depends on severity) or (**ceftriaxone** 2 gm q24h IV < age 60 1 gm q24h IV > age 60)		Small ↑ in incidence in Netherlands where use of antibiotics limited to children with complicated course or high risk *(PIDJ 20:140, 2001)*
Chronic	Often polymicrobic anaerobes S aureus Enterobacteriaceae P aeruginosa	Treatment for acute exacerbations or perioperatively Ideally no treatment until surgical cultures obtained Examples of empiric regimens **IMP** 0.5 gm q6h IV **TC/CL** 3.1 gm q6h IV **PIP/TZ** 3.375 gm q4–6h or 4.5 gm q8h IV		May or may not be associated with chronic otitis media with drainage via ruptured tympanic membrane Antimicrobials given in association with surgery Mastoidectomy indications chronic drainage and evidence of osteomyelitis by MRI or CT evidence of spread to CNS (epidural abscess suppurative phlebitis brain abscess)
EYE—General Reviews: ***CID 21:479, 1995; IDCP 7:447, 1998***				
Eyelid				
Blepharitis	Etiol unclear Factors include Staph aureus & Staph epidermidis seborrhea rosacea & dry eye	Lid margin care with baby shampoo & warm compresses qd Artificial tears if assoc dry eye *(see Comment)*		Usually topical ointments of no benefit If associated rosacea add doxy 100 mg po bid x2 wks and then qd
Hordeolum (Stye)				
External (gland of Zeis)	Staph aureus	Hot packs only Will drain spontaneously		Infection of superficial sebaceous gland
Internal (Meibomian glands)	Staph aureus	Oral **nafcillin/oxacillin** + hot packs		Also called acute meibomianitis Rarely drains spontaneously
Conjunctiva: *NEJM 343:345, 2000*				
Conjunctivitis of the newborn (**ophthalmia neonatorum**) by day of onset post delivery—all doses pediatric				
Onset 1st day	Chemical due to $AgNO_3$ prophylaxis	None		Usual prophylaxis is erythro ointment hence $AgNO_3$ irritation rare
Onset 2–4 days	N gonorrhoeae	**Ceftriaxone** 25–50 mg/kg IV x1 dose *(see Comment)* not to exceed 125 mg		Treat mother and her sexual partners Hyperpurulent Topical rx inadequate **Treat neonate for concomitant Chlamydia trachomatis.**
Onset 3–10 days	Chlamydia trachomatis	**Erythro eyrup** 50 mg/kg/d (po in 4 div doses x14 d) No topical rx needed		Diagnosis by antigen detection Azithro susp 20 mg/kg po qd x3 d reported efficacious *(PIDJ 17:1049, 1998)* Treat mother & sexual partner
Onset 2–16 days	Herpes simplex types 1, 2	*See keratitis, next page*		Consider IV acyclovir if concomitant systemic disease
Ophthalmia neonatorum prophylaxis **Silver nitrate** 1% x1 or **erythro** 0.5% ointment x1 or **tetra** 1% ointment x1 application				
Pink eye (viral conjunctivitis) Usually unilateral	Adenovirus (types 3 & 7 in children, 8, 11 & 19 in adults)	No treatment If symptomatic cold artificial tears may help		Highly contagious Onset of ocular pain and photophobia in an adult suggests associated keratitis—rare
Inclusion conjunctivitis **(adult)** Usually unilateral	Chlamydia trachomatis	**Doxy** 100 mg bid po x1–3 weeks	**Erythro** 250 mg qid po x1–3 weeks	Oculogenital disease Diagnosis by culture or antigen detection or PCR—availability varies by region and institution Treat sexual partner
Trachoma	Chlamydia trachomatis	**Azithro** 20 mg/kg po single dose—78% effective in children	**Doxy** 100 mg bid po x14 d or **tatracycline** 250 mg qid po x14 d	Starts in childhood and can persist for years with subsequent damage to cornea Topical therapy of marginal benefit Avoid doxy/tetracycline in young children Ref *CID 24:363, 1997* Mass treatment works *(JAMA 292:721, 2004)*
Suppurative conjunctivitis				
Non-gonococcal non-chlamydial *Med Lett 46:25, 2004*	Staph aureus S pneumoniae H influenzae et al Outbreak due to atypical S pneumo *NEJM 348:1112, 2003*	Ophthalmic solution Gati 0.3% Levo 0.5% or Moxi 0.5% All 1–2 gtts q2h while awake 1st 2 days then q4–8h up to 7 d	Polymyxin B + trimethoprim solution 1–2 gtts q3–6h x7–10 d	FQs best spectrum for empiric therapy but expensive $40–50 for 5 ml High concentrations ↑ likelihood of activity vs S aureus—even MRSA TMP spectrum may include MRSA Polymyxin B spectrum only Gm-neg bacilli but no ophthal prep of only TMP Most S pneumo resistant to gent & tobra
Gonococcal (peds/adults)	N gonorrhoeae	**Ceftriaxone** 125 mg IM or IV as one dose in children 1 gm IM/IV as one dose in adults		

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (6)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
EYE *(continued)*				
Cornea (keratitis):	**Usually serious and often sight-threatening. Prompt ophthalmologic consultation essential! Herpes simplex most common etiology in developed countries; bacterial and fungal infections more common in underdeveloped countries**			
Viral				
H simplex	H simplex types 1 & 2	**Trifluridine** one drop qh 9x/d for up to 21 days	**Vidarabine** ointment—useful in children Use 5x/d for up to 21 days	Fluorescein staining shows topical dendritic figures 30–50% rate of recurrence within 2 years 400 mg acyclovir po bid ↓ recurrences p 0 005 *(NEJM 339 300 1998)* If child fails vidarabine try trifluridine
Varicella-zoster ophthalmicus	Varicella-zoster virus	**Famciclovir** 500 mg tid po or **valacyclovir** 1 0 gm tid po x10 days	**Acyclovir** 800 mg po 5x/day x10 days	Clinical diagnosis most common dendritic figures with fluorescein staining in patient with varicella-zoster of ophthalmic branch of trigeminal nerve
Bacterial		***All rx listed for bacterial, fungal, & protozoan is topical***		
Contact lens users	P aeruginosa	**Tobra** or **gentamicin** (14 mg/ml) + **piperacillin** or **ticarcillin** eye drops (6–12 mg/ml) q15–60 min around clock x24–72 hrs then slow reduction	**CIP** 0 3% or **Levo** 0 5% drops q15–60 min around clock x24–72 hrs	Pain photophobia impaired vision Recommend alginate swab for culture and sensitivity testing
Dry cornea diabetes immunosuppression	Staph aureus S epidermidis, S pneumoniae S pyogenes, Enterobacteriaceae listeria	**Cefazolin** (50 mg/ml) + **gentamicin** or **tobra** (14 mg/ml) q15–60 min around clock x24–72 hrs then slow reduction	**Vanco** (50 mg/ml) + **ceftazidima** (50 mg/ml) q15–60 min around clock x24–72 hrs then slow reduction *See Comment*	Specific therapy guided by results of alginate swab culture and sensitivity CIP 0 3% found clinically equivalent to cefazolin + tobra only concern was efficacy of CIP vs S pneumoniae *(Ophthalmology 163 1854 1996)*
Fungal	Aspergillus fusarium candida No empiric therapy—*see Comment*	**Natamycin** (5%) drops q4–3 hrs with subsequent slow reduction	**Ampho B** (0 05–0 15%) q4–3 hrs with subsequent slow reduction	No empiric therapy Wait for results of Gram stain or culture in Sabouraud's medium
Protozoan Soft contact lens users (overnight use ↑ risk 10–15 fold)	Acanthamoeba hartmannella	**Propamidine** 0 1% + **neomycin/gramicidin/polymyxin** Eyedrops q waking hour x1 week and then slow taper	**Polyhexamethylene biguanide (PHMB)** 0 02% or **chlorhexidine** 0 02%	Uncommon Trauma and soft contact lenses are risk factors Corneal scrapings stained with calcofluor white show characteristic cysts with fluorescent microscopy PHMB source Leiter's Park Ave Pharm 800 292 6773 Ref *CID 35 434 2002*
Lacrimal apparatus				
Canaliculitis	Actinomyces most common Rarely Arachnia fusobacterium nocardia candida	Remove granules & irrigate with **pen G** (100 000 µg/ml) **Child: AM/CL** or **O Ceph 2**	If fungi irrigate with **nyatatin** approx 5 µg/ml + 1 gtt tid	Digital pressure produces exudate at punctum Gram stain confirms diagnosis Hot packs to punctal area qid
Dacryocystitis (lacrimal sac)	S pneumo, S aureus H influenzae S pyogenes P aeruginosa	Often consequence of obstruction of lacrimal duct Empiric rx based on Gram stain of aspirate—see *Comment*		Need ophthalmologic consultation Can be acute or chronic Culture to detect MRSA
Endophthelmitis For post-op endophthalmitis *see CID 38 542 2004* Bacterial Haziness of vitreous key to diagnosis Needle aspirate of both vitreous and aqueous humor for culture prior to therapy Intravitreal administration of antimicrobials essential				
Postocular surgery (cataracts) Early acute onset (incidence 0 05%)	S epidermidis 60% Staph aureus streptococci & enterococci each 5–10% Gm-neg bacilli 6%	**Immediate ophthal. consult.** If only light perception or worse immediate vitrectomy + intravitreal vanco 1 mg & intravitreal ceftazidime 2 25 mg No clear data on intravitreal steroid May need to repeat intravitreal antibiotics in 2–3 days Can usually leave lens in		
Low grade chronic	Propionibacterium acnes S epidermidis, S aureus (rare)	May require removal of lens material Intraocular **vanco** ± vitrectomy		

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (9)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
EYE/Endophthalmitis/Bacterial *(continued)*				
Post filtering blebs for glaucoma	Strep species (viridans & others), H influenzae	Intravitreal and topical agent and consider systemic **AM/CL**, **AM/SB** or **P Ceph 2**		
Post-penetrating trauma	Bacillus sp, S epiderm	Intravitreal agent as above + systemic **clinda** or **vanco**. Use topical antibiotics post surgery (tobra & cefazolin drops)		
None, suspect hematogenous	S pneumoniae, N meningitidis, Staph aureus	**P Ceph 3** (**cetotaxime** 2.0 gm q4h IV or **ceftriaxone** 2.0 gm q24h IV) + **vanco** 1.0 gm q12h IV pending cultures. Intravitreal antibiotics as with early post-operative		
IV heroin abuse	Bacillus cereus, Candida sp	Intravitreal agent + (systemic **clinde** or **vanco**)		
Mycotic (fungal). Broad-spectrum antibiotics, often corticosteroids, indwelling venous catheters	Candida sp, Aspergillus sp	Intravitreal **ampho B** 0.005–0.010 mg in 0.1 ml. *Also see Table 11, pages 74–76 for concomitant systemic therapy. See Comment*		With moderate/marked vitritis, options include systemic rx + vitrectomy ± intravitreal ampho B *(CID 27:1130 & 1134, 1998)*. Report of failure of ampho B lipid complex *(CID 28:1177, 1999)*
Retinitis				
Acute retinal necrosis	Varicella zoster, Herpes simplex	IV **acyclovir** 10–12 mg/kg IV q8h x5–7 d, then 800 mg po 5x/d x6 wks		Strong association of VZ virus with atypical necrotizing herpetic retinopathy *(CID 24:603, 1997)*
HIV+ (AIDS). *CD4 usually <100/mm³*	Cytomegalovirus	*See Table 14, page 107*		Occurs in 5–10% of AIDS patients
Orbital cellulitis *(see page 36 for erysipelas, facial)*	S pneumoniae, H influenzae, M catarrhalis, S aureus, anaerobes, group A strep, occ Gm-neg bacilli post trauma	**P Ceph 2/3** (**cefuroxime** 1.5 gm q8h IV, **cetoxitin** 2.0 gm q8h IV, **cefotetan** 2.0 gm q12h IV) or **AM/SB** 1.5 gm q6h IV	**TC/CL** or **PIP/TZ** *(see footnote[1] for dosages)* or **cefotaxime** 2.0 gm q4h IV or **ceftriaxone** 2.0 gm q24h IV	*See mucor/rhizopus, Table 11, page 80*. H influenzae becoming a rare etiology
FOOT				
"Diabetic". Reviews *NEJM 351:48, 2004; Ln 361:1545, 2003; CID 39:S73 & S104, 2004*				
Ulcer without bacterial invasion	Colonizing skin flora	Glucose control, ↓ weight-bearing, no antibiotic		**2/3 of pts have peripheral vascular disease; assess early & revascularize if possible.** 80% of pts have peripheral neuropathy. Determine if osteomyelitis present *(see Contiguous osteo, page 2)* **Principles of treatment:** (1) Revascularize if needed & possible. (2) Eradicate infection if present. (3) Remove pressure on ulcer. Best method is a non-removable total contact cast. **Notes:** (1) Charcot foot ret *Ln 360:1776, 2002*. (2) ERTA not active vs P aeruginosa. (3) Linezolid superior to AM/SB in 1 study *(CID 38:17, 2004)*
Mild, small, only skin, no inflammation, pulses present	**Polymicrobic:** S aureus (includes MRSA), Strep species, coliforms, anaerobic bacteria	Glucose control, non-invasive vascular studies, superficial ulcer swabs not helpful. **Rx:** (**TMP/SMX-DS** 1 tab po bid or **AM/CL-ER** 2000/125 bid) x1–2 wks. Some add **RIF** 300 mg bid to TMP/SMX-DS		
Severe—limb-threatening skin, subcutaneous, maybe bone inflammation, fever, neutrophilia		Glucose control, debridement with cultures & then (**IMP** or **MER** or **ERTA** or **PIP/TZ**) + (**vanco** or **linezolid**). *Dosages in footnotes[1 & 2]*		
Onychomycosis *See Table 11, page 78, fungal infections*				
Puncture wound: Nail	P aeruginosa	Cleanse, Tetanus booster, Observe		*See page 2*. 1–2% evolve to osteomyelitis. Other organisms if tooth pick in urine *(PIDJ 23:80, 2004)*
GALLBLADDER				
Cholecystitis, cholangitis, biliary sepsis or common duct obstruction (partial 2nd to tumor, stones, stricture)	Enterobacteriaceae 68%, enterococci 14%, bacteroides 10%, Clostridium sp 7%, rarely candida	**PIP/TZ** or **AM/SB** or **TC/CL** or **ERTA** or **MER**. If life-threatening **IMP**	**P Ceph 3** + **metro** OR **Aztreonam** + **metro** OR **CIP** + **metro**. *Dosages in footnote[2]*	For severely ill pts, antibiotic rx is complementary to adequate biliary drainage. 15–30% pts will require decompression: surgical, percutaneous or ERCP placed stent. Whether empirical rx should always cover pseudomonas & anaerobes is uncertain *(CID 19:279, 1994)*. Ceftriaxone associated with biliary sludge (by ultrasound 50%, symptomatic 9% *NEJM 322:1821, 1990*), clinical relevance still unclear, but has led to sur[illegible] *MMWR 42:39, 1993*

[1] **Cephalexin** 500 mg po qid. **cefoxitin** 2.0 gm q8h IV. **CIP** 750 mg bid po or 400 mg bid IV. **Lavo** 750 mg po qd. **clinda** 300 mg qid po or 450–900 mg q8h IV. **IMP** 0.5 gm q6h IV. **MER** 1.0 gm q8h IV. **AM/CL** 875/125 mg q12h or 500/125 mg tid or 2000/125 bid po. **TC/CL** 3.1 gm q6h IV. **PIP/TZ** 3.375 gm q6h or 4.5 gm q8h IV. **AM/SB** 3.0 gm q6h IV. **aztreonam** 2.0 gm q8h IV. **FO IV** (**CIP** 400 mg q12h, **Gati** 400 mg q24h, **Otlox** 400 mg q12h). **Vanco** 1.0 gm IV q12h. **Linezolid** 600 mg po q12h.

[2] **AP Pen** (**ticarcillin** 4.0 gm q6h IV, **PIP** 4.0 gm q6h IV), **metro** 1.0 gm IV loading dose then 0.5 gm q6h or 1.0 gm q12h IV. **ERTA** 1.0 gm IV qd. **IMP** 0.5 gm q6h IV. **MER** 1.0 gm q8h IV. **TC/CL** 3.1 gm q6h IV. **PIP/TZ** 3.375 gm q6h or 4.5 gm q8h IV. **AM/SB** 3.0 gm q6h IV. **AMP** 2.0 gm q6h IV. *see previous footnote for* **clinda** *and* **aztreonam** *dosage*. **P Ceph 3** *dose in Table 10B, pages 67, 68*. **CIP** 400 mg IV q12h. **Lavo** 750 mg IV qd. **vanco** 1.0 gm IV q12h. **metro** 500 mg po qid or 15 mg/kg IV q12h (max 4 gm/d). **linezolid** 600 mg IV q12h.

(Footnotes and abbreviations on page 45) *NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GASTROINTESTINAL				
Gastroenteritis—Empiric Therapy (laboratory studies not performed or culture, microscopy, toxin results NOT AVAILABLE) (Ref *NEJM 350 38 2004*)				
Premature infant with necrotizing enterocolitis	Associated with intestinal flora	Treatment and rationale as for diverticulitis/peritonitis *page 14. See Table 16 page 131 for pediatric dosages*		Pneumatosis intestinalis on x-ray confirms dx Bacteremia-peritonitis in 30–50% If Staph epidermidis isolated add vanco (IV)
Mild diarrhea (≤3 unformed stools/day, minimal associated symptomatology)	Bacterial (*see Severe, below*), viral parasitic Viral usually causes mild to moderate disease For traveler's diarrhea *see page 13*	Fluids only + lactose-free diet avoid caffeine		**Rehydration: For po fluid replacement, see Cholera, page 12.** ***Antimotility:*** Loperamide (Imodium) 4 mg po then 2 mg after each loose stool to max of 16 mg/day Bismuth subsalicylate (Pepto Bismol) 2 tablets (262 mg) po qid Do not use if suspect hemolytic uremic syndrome
Moderate diarrhea (≥4 unformed stools/day and/or systemic symptoms)		Antimotility agents *(see Comments)* + fluids		***Hemolytic uremic syndrome (HUS):*** Risk in **children** infected with E coli 0157 H7 is 8–10% Early treatment with TMP/SMX or FQs ↑ risk of HUS *(NEJM 342 1930 & 1990 2000)* Controversial meta-analysis *JAMA 288 996 & 3111 2002*
Severe diarrhea (≥6 unformed stools/day and/or temperature ≥101°F, tenesmus blood or fecal leukocytes) **NOTE: Severe afebrile bloody diarrhea should ↑ suspicion of *E. coli* 0157:H7 infection**—causes only 1–3% all cases diarrhea in U S —but causes up to 36% cases of bloody diarrhea *(CID 32 573, 2001)*	Shigella salmonella C jejuni E coli 0157 H7 toxin-positive C difficile E histolytica *For typhoid fever see page 41*	**FQ** (**CIP** 500 mg q12h po or **Levo** 500 mg qd) x3–5 days	**TMP/SMX-DS** bid po x3–5 days Campylobacter resistance to TMP/ SMX common in tropics	***Other potential etiologies:*** Cryptosporidia—no treatment in immunocompetent host *(see Table 13A & JID 170 272 1994)* Cyclospora—usually chronic diarrhea responds to TMP/SMX *(see Table 12A & AIM 123 409 1995)* ***Severe diarrhea*** treated with CIP 500 mg bid po decreases duration of diarrhea and other symptoms without changing duration of fecal carriage 10% campylobacter in Minn resistant to FQs *(NEJM 340 1525, 1999)*
		If recent antibiotic therapy (C difficile toxin colitis possible) **add**		
		Metro 500 mg tid po x10–14 days	**Vanco** 125 mg qid po x10–14 days	
Gastroenteritis—Specific Therapy (results of culture, microscopy, toxin assay AVAILABLE)- Ref *NEJM 350 38 2004*				
If culture negative probably **Norovirus (Norwalk)** or rarely (in adults) **Rotavirus**—see *Table 14A page 111*	**Aeromonas/plesiomonas**	**CIP** 500 mg po bid x3 d	**TMP/SMX-DS** po bid x3 d	Although no absolute proof increasing evidence as cause of diarrheal illness
	Amebiasis (Entamoeba histolytica, Cyclospora, Cryptosporidia and **Giardia), see *Table 13A***			
	Campylobacter jejuni CAUTION *See Comment on FQ resistance* Fever in 53–83% H/O[1] bloody stools 37%	**Azithro** 500 mg po qd x3 d or **CIP** 500 mg po bid *(See Comment)*	**Erythro stearate** 500 mg qid po x5 d	↑ **worldwide resistance to FOs** varies by region from 10% (USA) to 84% (Thailand) *(AAC 47 2358, 2003)* Erythro resistance rarely reported *(CID 37 131 2003)* Post-Campylobacter Guillain Barre assoc 15% of cases *(CID 37 307, 2003)* Assoc with small bowel lymphoproliferative disease may respond to antimicrobials *(NEJM 350 239, 2003)*
	C. difficile toxin positive antibiotic associated colitis (Ref *NEJM 346 334 2002)* **Remember: contact isolation indicated** Fever in 28% **Diagnosis:** Tissue culture—detects toxin A&B most sensitive Takes 48 hrs Rapid immunoassays Less sens detect toxin A, B, or both 10–20% false-neg rate	**Metro** 500 mg tid or 250 mg qid po x10–14 d Rare reports of in vitro resistance to metro *(AAC 46 1647, 2002)*	(**Vanco** 125 mg qid po) or (**bacitracin** 25 000 u qid po) or (**cholestyremine** 4 gm tid po) x10–14 d **Teicoplanin**[NUS] 400 mg po 2x/d x10 d	**DC antibiotic if possible; avoid antimotility agents; hydration; enteric isolation.** **Relapse occurs in 10–20%;** First re-treat with **metro** For refractory disease **vanco** po + **RIF** po reported effective *(ICHE 16 459 1995)* **metro + RIF** should work but no published data **Other relapse rx regimens: metro** x10 d then (**cholestyramine** 4 gm po tid + **lactobacillus** 1 gm qid) x4 wks **OR vanco** 125 mg po qod x4 wks **OR vanco taper** all doses 125 mg po week 1—qid week 2—bid week 3—qd, week 4—qod, weeks 5 & 6 q 3 days **When po rx not possible**, use IV metro + vanco 500 mg/L saline via small bowel tube and/or via pigtail catheter in cecum (in severe typhlitis pts) Perfuse at 1–3 ml/min to daily max of 2 0 gm *see NEJM 329 583 1993 & CID 35 690, 2002* **NOTE: IV vanco not effective.** Unclear how much IV metro gets to colonic mucosa & colonic content hence combination of IV metro & po (or via tube) vanco
		If too ill for po rx **metro** 500 mg q6h IV (efficacy not established) if ileus, add **vanco** by N-G or naso-small bowel tube *(see Comment)* &/or retrograde cecal catheter &/or **vanco** enemas *(see Comment)*	For relapses (**metro** 500 mg tid po + **RIF** 300 mg bid po) x10 d *(see Comment)*	

[1] **H/O** = history of

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (11)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
Gastrointestinal/Gastrosnteritis—Specific Therapy *(continued)*				
	E. coli 0157:H7 Fever in 16–45% H/O[1] bloody stools 63%	**NO TREATMENT** with antimicrobials or anti-motility drugs, as may enhance toxin release and ↑ risk of hemolytic uremic syndrome (HUS) *(NEJM 342 1930 & 1990 2000)* Rehydration important		NOTE 5–10% of pts develop HUS (approx 10% with HUS die or have permanent renal failure 50% HUS pts have some degree of renal impairment *(CID 38 1298, 2004)*
	Listeria monocytogenes	**AMP** 200 mg/kg/d IV div q6h	**TMP/SMX** 20 mg/kg/d IV div q6–8h	Recently recognized cause of food poisoning manifest as febrile gastroenteritis Percentage with complicating bacteremia/meningitis unknown Not detected in standard stool culture *(NEJM 336 100 & 130, 1997)*
	Salmonella, non-typhi— For typhoid fever, *see page 41* Fever in 71–91%, H/O[1] bloody stools in 34%	If pt asymptomatic or illness mild, antimicrobial therapy not indicated Treat if <1 yr old or >50 yrs old if immunocompromised if vascular grafts or prosthetic joints *(see typhoid fever page 41)*		
		CIP 500 mg po bid x5–7 d Resistance ↑ *(Ln 353 1590 1999)*	**Azithro** 1 0 gm po once then 500 mg qd x6 d *(AAC 43 1441 1999)*	↑ resistance to TMP/SMX and chloro Ceftriaxone cefotaxime usually active *(see footnote page 16 for dosage)* ceftriaxone & FO resistance in SE Asia *(EID 9 255 & 323 2003 Ln 363 1285, 2004)* Primary treatment of enteritis is fluid and electrolyte replacement No adverse effects from FOs in children *(Ln 348 547 1996)* If immunocompromised rx 14 d
	Shigella Fever in 58% H/O[1] bloody stools 51%	**FQs** po (**CIP** 500 mg bid) or (**Levo** 500 mg qd)—x3 d	(**TMP/SMX-DS** bid po x3 d) or (**azithro** 500 mg po x1 then 250 mg qd x4 d)	**Peds dosea:** TMP/SMX 5/25 mg/kg po x3 d For severe disease ceftriaxone 50–75 mg/kg/d x2–5 d CIP suspension 10 mg/kg bid x5 d *(Ln 352 522 1998)* CIP superior to ceftriaxone in children *(LnID 3 537 2003)* **Immunocompromised children & adults: Treat for 7–10 d.** Azithro superior to cefixime[NUS] in trial in children *(PIDJ 22 374, 2003)*
		See Comment for peds rx/dose		
	Vibrio cholerae Treatment decreases duration of disease vol losses and duration of excretion *CID 37 272 2003 Ln 363 223 2004*	**CIP** 1 0 gm po x1 + fluids **Primary rx is hydration** *(see Comment)*	**Doxy** 300 mg po x1 + fluids *(see Comment)* For children <8 yrs & in pregnancy **TMP/SMX-DS** one bid po x3 d or for Peds alternative **azithro** x1—*see dose in Comment*	Primary rx is fluid **IV** use (per liter) 4 gm NaCl 1 gm KCl 5 4 gm Na lactate 8 gm glucose **PO** use (per liter potable water) 1 level teaspoon table salt + 4 heaping teaspoons sugar *(JTMH 84 73 1981)* Add orange juice or 2 bananas for K Volume given = fluid loss Mild dehydration give 5% body weight for moderate 7% body weight (Refs *CID 20 1485 1995 TRSM 89 103 1995)* Peds azithro 20 mg/kg (to 1 gm max) x1 *(Ln 360 1722 2002)*
	Vibrio parahaemolyticus	Antimicrobial rx does not shorten course		Sensitive in vitro to FQ doxy Often history of seafood ingestion
	Vibrio vulnificus	Usual presentation is skin lesions & bacteremia *see page 37*		
	Yersinia enterocolitica Fever in 68% bloody stools in 26%	No treatment unless severe If severe combine **doxy** 100 mg IV bid + (**tobra** or **genta** 5 mg/kg/d once daily) **TMP/SMX** or **FQs** are alternatives		Mesenteric adenitis pain can mimic acute appendicitis Lab diagnosis difficult requires 'cold enrichment' and/or yersinia selective agar Desferrioxamine rx ↑ severity discontinue it pt on it Iron overload states predispose to yersinia *(CID 27 1362 & 1367 1998)*
Gastroenteritis—Specific Risk Groups–Empiric Therapy				
Anoreceptive intercourse				
Proctitis (distal 15 cm only)	Herpes viruses gonococci chlamydia syphilis *See Genital Tract page 15*			
Colitis	Shigella salmonella campylobacter E histolytica *(see Table 13A)*	**FO** (e g **CIP** 500 mg q12h po) x3 d		
HIV-1 infected (AIDS): >10 days diarrhea	G lamblia			*See Table 13A*
Acid-fast organisms	Cryptosporidium parvum Cyclospora cayetanensis			*See Table 13A* For influence of highly active antiretroviral therapy *see CID 28 701 1999*
Other	Isospora belli microsporidia (Enterocytozoon bieneusi Septata intestinalis)			*See Table 13A*
Neutropanic enterocolitis or "typhlitis" *(CID 27 695 & 700 1998)*	Mucosal invasion by **Clostridium aapticum** Occasionally caused by C sordelli or P aeruginosa	As for perirectal abscess Ensure empiric regimen includes drug active vs Clostridia species e g **pen G AMP** or **clinda** *(see Comment re resistance)* Empiric regimen should have predictive activity vs P aeruginosa also		Tender right lower quadrant Surgical resection controversial but may be necessary **NOTE:** Resistance of clostridia to clindamycin reported

[1] **H/O** = history of

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (12)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
Gastrointestinal/Gastroenteritis—Specific Risk Groups—Empiric Therapy *(continued)*				
Traveler's diarrhea self-medication Patient usually afebrile *(NEJM 342 1716 2000)*	**Acute** 60% due to toxigenic E coli shigella salmonella or campylobacter C difficile amebiasis *(see Table 13)* **If chronic** cyclospora cryptosporidia, giardia isospora	**Azithro** 1 0 gm po x1 dose or **rifaximin** 200 mg po tid x3 d	**Levo** 500 mg po x1 dose Alternative **CIP** or **other FQ** bid x3 d *(see footnote[1])*	Treatment based on randomized trial *(CID 37 1165 2003)* Peds & pregnancy Avoid FQs Azithro peds dose 5–10 mg/kg x1 dose Rifaximin approved for age 12 or older Adverse effects similar to placebo
		Imodium optional 4 mg x1 then 2 mg after each loose stool to max 16 mg/d		No loperamide if fever or blood in stool
Prevention	Not routinely indicated Current recommendation is to take **FQ** + **Imodium** with 1st loose stool *(NEJM 328 1821 1993)*		Alternative during 1st 3 weeks only if activities are essential Options **Bismuth subsalicylate** (Pepto Bismol) 2 tabs (262 mg) po qid or **FQ—CIP** 500 mg po qd **Bismuth subsalicylate** can cause black tongue and dark stool	
Gastrointestinal Infections by Anatomic Site				
Esophagitis	Candida albicans HSV CMV	*See SANFORD GUIDE TO HIV/AIDS THERAPY*		
Duodenal/Gastric ulcer, gastric cancer MALT lymphomas (not 2 NSAIDs) *(NEJM 347 1175 2002 Can J Gastro 17 25B 2003)*	**Helicobacter pylori** *See Comment* Prevalence of pre treatment resistance increasing	**Rx 2x/day po for 14 days: (Omeprazole or rabaprazole** 20 mg)[2] + **amox** 1 gm + **clarithro** 500 mg Efficacy 80–95%	**Rx po for 14 days: Bismuth** *(see footnote[3])* bismuth subsalicylate 2 tabs 4x/d + **tetracycline** 500 mg 4x/d + **metro** 500 mg 3x/d + **omaprazole**[2] 20 mg 2x/d Efficacy 90–99%	**Dx: Stool antigen**—>90% sens & specific Cheap & practical Rare false-pos due to other Helicobacter species *(BMJ 320 148 2000)* Other tests Urea breath test if endoscoped rapid urease &/or histology &/or culture **Antimicrobial resistance: Predicts rx failure** *(Antim 139 463 2003)* Geographic differences but overall resistance amox & tetra uncommon clarithro 10% metro 30–50% **Treatment success:** Correlates with active drugs & pt compliance Suggested **rx duration** varies between 7–14 d we suggest bid regimen x14 d to ↑ compliance & hopefully efficacy (7–9% ↑ cures with 14 d) *(Ailment Pharmacol Ther 14 603 2000)* **Test of cure:** Repeat stool antigen >8 wks post treatment
Whipple's disease *(CID 32 457 2001 Ln 363 654 2004)* *See Infective endocarditis culture-negative page 20*	Trophermyma whippelii	**Initial 10–14 days (Pen G** 6–24 mill U IV qd + **streptomycin** 1 0 gm IM/IV qd) OR **ceftriaxone** 2 0 gm IV qd	**TMP/SMX-DS** 1 tab po bid	Rx regimen based on empiricism and retrospective analyses TMP/SMX CNS relapses during TMP/SMX rx reported Interesting in vitro susceptibility study combination of doxy & hydroxychloroquine bactericidal *(AAC 48 747 2004)*
		Than, for approx. 1 year TMP/SMX-DS 1 tab po bid	**(Doxy** 100 mg po bid) or (**cefixime**[NUS] 400 mg po bid) or (**Pen VK** 500 mg po qid)	
Inflammatory bowel disease: Ulcerative colitis Crohn's disease Mild to moderate Ref *Ln 359 331 2002*	Unknown	**Sulfasalazine** 1 0 gm q6h po or **mesalamine (5ASA)** 1 0 gm q6h po	**Coated mesalamine** (Asacol) 800 mg bid or qid equally effective Corticosteroid enemas	Check stool for E histolytica Try aminosalicylates 1st in mild/mod disease See review article for more aggressive therapy
	In randomized controlled trial CIP + metro had no benefit *(Gastro 123 33 2002)*			
Severe Crohn's	Unknown	Etanercept	Infliximab/adalimumab	Screen for latent TBc before blocking TNF *(MMWR 53 683 2004)*

[1] **FQ** dosage po for self-rx traveler's diarrhea—mild disease **CIP** 750 mg x1 severe 500 mg bid x3 d **Oflox** 300 mg po bid x3 d Once daily **Levo** 500 mg **Gati** or **Moxi** 400 mg x3 d probably would work but not FDA-approved indication

[2] Can substitute other **proton pump inhibitors** for omeprazole or rabeprazole—all bid esomeprazole 20 mg *(FDA-approved)* lansoprazole 30 mg *(FDA-approved)* pantoprazole 40 mg *(not FDA-approved for this indication)*

[3] **3 bismuth preparations:** (1) In U S **bismuth subsalicylate (Pepto-Bismol)** 262 mg tabs adult dose for helicobacter is 2 tabs (524 mg) 4x/day (2) Outside U S colloidal bismuth subcitrate (De-Nol) 120 mg chewable tablets dose is 1 tablet 4x/day (3) Another treatment option Ranitidine bismuth citrate 400 mg give with metro 500 mg and clarithro 500 mg—all bid x7 d Worked despite metro/clarithro resistance *(Gastro 114 A323, 1998)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (13)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE‡	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GASTROINTESTINAL/Gastrointestinal infections by anatomic site *(continued)*				
Diverticulitis, perirectal abscess, peritonitis *Also see Peritonitis, page 31 CID (in press)*	Enterobacteriaceae, occ P aeruginosa Bacteroides sp enterococci	**Outpatient rx—mild diverticulitis, drained peri-rectal abscess:** [(**TMP/SMX-OS** bid) or (**CIP** 750 mg bid or **Levo** 750 mg 1x/d)] + **metro** 500 mg q6h All po x7–10 d	**AM/CL-ER** 1000/62 5 mg 2 tabs po bid x7–10 d	Must "cover" both Gm-neg aerobic and Gm-neg anaerobic bacteria **Druge active only va anaerobic Gm-neg. bacilli:** clinda, metro **Orugs active only ve aerobic Gm-neg. bacilli:** APAG¹, P Ceph 2/3/4 aztreonam AP Pen CIP Levo **Druga active va both aerobic/aneerobic Gm-neg. bacteria:** cefoxitin cefotetan TC/CL PIP/TZ, AM/SB ERTA IMP, MER Gati & Moxi Increasing resistance of Bacteroides species **Cefoxitin** **Cefotetan** **Clindamycin** % Resistant 4–25 17–87 16–44 Essentially no resistance metro PIP/TZ *[CID 35(Suppl 1) S126, 2002]* **Ertapanam** less active vs P aeruginosa/Acinetobacter sp than IMP or MER **Concomitant surgical management important** esp with moderate-severe disease **Role of enterococci remains debatable** Probably pathogenic in infections of biliary tract Probably need drugs active vs enterococci in pts with valvular heart disease
		Mild-moderate disease—Inpatient—Parenteral Rx: (e g local peri-appendiceal peritonitis, peri-diverticular abscess endomyometritis) **PIP/TZ** 3 375 gm IV q6h or 4 5 gm IV q8h **or AM/SB** 3 gm IV q6h **or TC/CL** 3 1 gm IV q6h **or ERTA** 1 0 gm IV qd	[(**CIP** 400 mg IV q12h) or (**Levo** 750 mg IV q24h)] + **metro** 500 mg IV q6h or 1 0 gm IV q12h *See Comment*	
		Severe life-threatening disease, ICU patient: IMP 500 mg IV q6h **or MER** 1 gm IV q8h	**AMP** + **metro** + (**CIP** 400 mg IV q12h or **Levo** 750 mg IV q24h) **OR** [**AMP** 2 gm IV q6h + **metro** 500 mg IV q6h + **APAG**¹ *(see Table 10C page 72)*]	**Severe penicillin/cephalosporin allergy:** (**aztreonem** 2 0 gm IV q6h) + [**metro** (500 mg IV q6h) or (1 0 gm IV q12h)] **OR** [(**CIP** 400 mg IV q12h) or (**Levo** 750 mg IV qd) + **metro**] Based on in vitro data, could sub **Gati/Moxi** for **CIP/Levo** but insufficient clinical data
GENITAL TRACT. Mixture of empiric & specific treatment. Divided by sex of the patient. For sexual assault (rape), see *Table 15A, page 123.* See Guidelines for Dx of Sexually Transmitted Diseases, *MMWR 51(RR-6), 2002* or *CID 35(Suppl.2):S135, 2002* or *www.cdc.gov/std/treatment/toc2002tg.htm*				
Both Women & Men:				
Chancroid *Ref CID 28(Suppl 1) S14, 1999*	H ducreyi	**Ceftriaxone** 250 mg IM single dose OR **azithro** 1 0 gm po single dose	**CIP** 500 mg bid po x3 d OR **erythro base** 500 mg qid po x7 d	In HIV+ pts failures reported with single dose azithro *(CID 21 409 1995)*
Chlamydia, et al. non-gonococcal or post-gonococcal urathritis, cervicitis **NOTE: Assume concomitant N. gonorrhoeae** Chlamydia conjunctivitis *see page 8*	Chlamydia 50% Mycoplasma hominis Other known etiologies (10–15%) Ureaplasma trichomonas herpes simplex virus Mycoplasma genitalium Chlamydia ref *NEJM 349 2424, 2003*	(**Doxy** 100 mg bid po x7 d) or (**azithro** 1 0 gm po as single dose) Evaluate & rx sex partner	(**Erythro base** 500 mg qid po x7 d) or (**Levo** 500 mg qd x7 d) **In pregnancy: erythro baae** 500 mg po qid x7 d OR **amox** 500 mg po tid x7 d	**Diagnosis:** Methods to detect C trachomatis & N gonorrhoeae summarized by CDC *MMWR 51 (RR-15) 1–39 2002* For C trachomatis a nucleic acid amplitest on urine urethral swab (men) or endocervical swab (women) suggested **For recurrent or persistent disease:** either metro 2 0 gm po x1 + either erythro base 500 mg po qid x7 d or erythro ethylsuccinate 800 mg po qid x7 d **Evaluate & treat sex partners.**
Recurrent/persistent urethritis	**Occult trichomonas** tetra resistant U urealyticum	**Metro** 2 0 gm po x1 + **erythro basa** 500 mg po qid x7 d	**In pregnancy: azithro** 1 0 gm po x1 **Doxy & Oflox contra-indicated** **Erythro ethyleuccinate** 800 mg po qid x7 d	In men with NGU 20% infected with trichomonas *(JID 188 465 2003)*
Gonorrhea *[MMWR 51(RR-6) 2002* or *CID 35 (Suppl 2) S135, 2002]*				
Conjunctivitis (adult)	N gonorrhoeae	**Ceftriaxone** 1 gm IM or IV x one dose		Consider saline lavage of eye x1

¹ **APAG = antipseudomonal aminoglycoside, e.g., amikacin, gentamicin, tobramycin**

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (14)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE§	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT/Both Women & Men/Gonorrhea *[MMWR 51(RR 6) 2002] (continued)*				
Disseminated gonococcal infection (DGI dermatitis arthritis syndrome)	N gonorrhoeae	(**Ceftriaxone** 1 0 gm IV qd) or (**cefotaxima** 1 0 gm q8h IV) or (**caftizoxime** 1 0 gm q8h IV)—*see Comment*	**Spectinomycin** 2 0 gm q12h IM or **CIP** 400 mg IV q12h or **Oflox** 400 mg IV q12h or **Levo** 250 mg IV daily—*see Comment*	Continue IM or IV regimen for 24 hrs after symptoms ↓ reliable pts may be discharged 24 hrs after sx resolve to complete 7 days rx with **cefixima**[NUS] **400 mg po bid or CIP 500 mg po bid or Oflox 400 mg po bid or Levo 500 mg po qd** R/O meningitis/ endocarditis **Treat preaumptively for concomitant C. trachomatis**
Endocarditis	N gonorrhoeae	**Ceftriaxone** 1–2 gm IV q12h x4 wks		
Pharyngitis	N gonorrhoeae	**Ceftriaxone** 125 mg IM x1	**CIP** 500 mg po x1 or **Levo** 250 mg po x1	If chlamydia not ruled out Azithro 1 gm po x1 or doxy 100 mg po bid x7 d Some suggest test of cure culture after 1 week Spectinomycin not effective
Urethritis, cervicitis, proctitis (uncomplicated) For prostatitis *see pages 17 18* **Diagnosis** Nucleic acid amplification test on urine or urethral swab—*see MMWR 51 (RR-15) 2002*	N gonorrhoeae (50% of pts with urethritis cervicitis have concomitant C trachomatis —**treat for both**)	[(**Ceftriaxone** 125 mg IM x1) or (**cefixime** 400 mg po x1) or **cefpodoxima** 400 mg po x1 or (**CIP** 500 mg po x1) or (**Oflox** 400 mg po x1) or (**Levo** 250 mg po x1) or **Geti** 400 mg po x1] **PLUS** [(**Azithro** 1 gm po x1) or (**doxy** 100 mg po 2x/d x7 days)] **NOTE** Due to resistance of approx 5% do not use FQs to treat (1) men who have sex with men or (2) GC acquired in Hawaii other Pacific areas or England Refs in Comments		**Treat for both GC and C. trachomatis.** Screen for syphilis Other alternatives for **GC:** Spectinomycin 2 gm IM x1 Other single-dose cephalosporins ceftizoxime 500 mg IM cefotaxime 500 mg IM cetoxitin 2 gm IM + probenecid 1 gm po Azithro 1 gm po x1 effective for chlamydia but need 2 gm po for GC not recommended for GC due to GI side-effects and expense FQ resistance refs *MMWR 53 335 2004 CID 38 649 2004*
Granuloma inguinale (Donovanosis)	Calymmatobacterium granulomatis	**Doxy** 100 mg bid po x3–4 wks OR **TMP/SMX-DS** 2x/d x3 wks	**Erythro** 500 mg qid po x3 wks OR **CIP** 750 mg po x3 wks OR **azithro** 1 0 gm po q wk x3 wks	Clinical response usually seen in 1 week Rx until all lesions healed may take 4 weeks Treatment failures & recurrence seen with doxy and TMP/SMX Report of efficacy with FQ and chloro Ref *CID 25 24 1997*
Herpes simplex virus	*See Table 14, page 108*			
Lymphogranuloma veneraum	Chlamydia trachomatis serovars L1 L2 L3	**Doxy** *100* mg bid po x21 d	**Erythro** 0 5 gm qid po x21 d	*Dx* based on serology biopsy contraindicated because sinus tracts develop Nucleic acid ampli tests in development
Phthirus pubis **(pubic lice, "crabs")** & scabies	Phthirus pubis & Sarcoptes scabiei	*See Table 13, page 100*		
Syphilis *(JAMA 290 1510 2003)*	**Syphilis & HIV:** *LnID 4 456 2004*			
Early primary, secondary or latent <1 year	T pallidum	**Benzathina pen G (Bicillin L-A)** 2 4 mU IM x1	(**Ooxy** 100 mg bid po x14 d) or (**tetracylina** 500 mg qid po x14 d) or (**caftriaxone** 1 0 gm IM/IV daily x8–10 d) Follow-up mandatory	If early or congenital syphilis **quantitate VDRL at 0** 3 6 12 & 24 months after rx If 1 or 2 syphilis, VDRL should ↓ 2 tubes at 6 months 3 tubes 12 months & 4 tubes 24 months Early latent 2 tubes ↓ at 12 months With 1° 50% will be RPR seronegative at 12 months 24% neg FTA/ABS at 2–3 yrs *(AnIM 114 1005, 1991)* **Azithro-resistant syphilis** documented in California Ireland & elsewhere *(NEJM 351 122 & 154 2004)*
More than 1 yr's duration (latent of indeterminate duration, cardiovascular late benign)		**Benzathine pen G (Bicillin L-A)** 2 4 mU IM q week x3 = 7 2 mU total	**Doxy** 100 mg bid po x28 d or **tetracycline** 500 mg qid po x28 d	No published data on efficacy of alternatives The value of routine lumbar puncture in asymptomatic late syphilis is being questioned in the U S I e no LP, rx all patients as primary recommendation *ArIM 145 465, 1985* **Indicationa for LP (COC): neurologic symptoms, treatment failure, aerum non-treponamal antibody titar ≥1:32, othar avidance of active syphilis (aortitis, gumma, iritis), non-penicillin rx, + HIV teat.**
Naurosyphilis—Very difficult to treat Includes ocular (retrobulbar neuritis) syphilis		**Pen G** 3–4 mU q4h IV x10–14 d	(**Procaine pen G** 2 4 mU qd IM + **probenecid** 0 5 gm qid po) both x10–14 d —*See Comment*	**Ceftriaxone** 2 0 gm qd (IV or IM) x14 d 23% failure rate reported *(AJM 93 481, 1992)* For penicillin allergy either desensitize to penicillin or obtain infectious diseases consultation **Serologic criteria for raaponse to rx: 4-fold or greeter ↓ in VDRL titer over 6–12 mos.** *[CID 28 (Suppl 1) S21, 1999]*

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (15)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT/Both Woman & Man/Syphilis *(continued)*				
HIV infection (AIDS) *(See SANFORD GUIDE TO HIV/AIDS THERAPY & refs in Comments)*	T pallidum	Adding 10 d of **amox** + **probenecid** to **pen G** did not change efficacy in 1 & 2 syphilis *(NEJM 337 307 1997)*	For neurosyphilis, recommendations vary some use **pen G** 24 mU qd IV for 14–21 d	HIV+ plus RPR ≥1 32 plus CD4 count ≤350/μl increases risk of neurosyphilis nearly 19-fold—examine CSF *(JID 189 369 2004)* also CSF changes less likely to normalize *(CID 38 1001 2004)* Review of syphilis & HIV *LnID 4 456, 2004*
Pregnancy and syphilis		Same as for non pregnant some recommend 2nd dose (2 4 mU) **benzathine pen G** 1 wk after initial dose esp in 3 d trimester or with 2 syphilis	Skin test for penicillin allergy Desensitize if necessary	Monthly quantitative VDRL or equivalent If 4 fold ↑ re-treat Doxy tetracycline contraindicated Erythro not recommended because of high risk of failure to cure fetus
Congenital syphilis		**Aqueous crystalline pen G** 50 000 u/kg/dose IV q8–12h x10–14 d	**Procaine pen G** 50 000 u/kg qd IM for 10 d	Another alternative Ceftriaxone ≤30 days old 75 mg/kg IV/IM qd or >30 days old 100 mg/kg IV/IM qd Treat 10–14 d If symptomatic, ophthalmologic exam indicated If more than 1 day of rx missed, restart entire course **Need serologic follow-up!**
Warts, anogenital	*See Table 14 page 111*			
Women:				
Amnionitis, septic abortion	Bacteroides esp Prevotella bivius Group B A strepto cocci Enterobacteriaceae C trachomatis	[(**Cefoxitin** or **TC/CL** or **IMP** or **MER** or **AM/SB** or **ERTA** or **PIP/TZ**) + **doxy**] **OR** [**Clinda** + (**APAG** or **P Caph 3**)] *Dosage see footnote†*		D&C of uterus **In septic abortion** Clostridium perfringens may cause fulminant intravascular hemolysis **In postpartum patients** with enigmatic fever and/or pulmonary emboli **consider septic pelvic vein thrombophlebitis** *(see Vascular septic pelvic vein thrombophlebitis page 44)* After discharge doxy or continue clinda **NOTE:** IV clinda effective for C trachomatis no data on po clinda *(CID 19 720 1994)*
Cervicitis, mucopuruient	N gonorrhoeae	Treat for gonorrhea *page 15*		Criteria for dx yellow or green pus on cervical swab >10 WBC/oil field Gram stain for GC, if negative rx for C trachomatis If in doubt send swab or urine for culture EIA or nucleic acid amplification test and rx for both
	Chlamydia trachomatis	Treat for non-gonococcal urethritis *page 14*		
Endomyometritis/aeptic pelvic phlebitis				
Early postpartum (1st 48 hrs) (usually after C section)	Bacteroides esp Prevotella bivius Group B A streptococci Enterobacteriaceae C trachomatis	[(**Cefoxitin** or **TC/CL** or **ERTA** or **IMP** or **MER** or **AM/SB** or **PIP/TZ**) + **doxy**] OR [**Clinda** + (**APAG** or **P Caph 3**)] *Dosage see footnote†*		*See Comments under Amnionitis septic abortion above*
Late postpartum (48 hrs to 6 wks) (usually after vaginal delivery	Chlamydia trachomatis M hominis	**Doxy** 100 mg q12h IV or po x14 d		Tetracyclines not recommended in nursing mothers discontinue nursing M hominis sensitive to tetra clinda not erythro *(CTID 17 5200 1993)*
Fitzhugh-Curtis syndroma	C trachomatis N gonorrheae	Treat as for pelvic inflammatory disease		Perihepatitis (violin string adhesions)
Pelvic inflammatory diseaae (PID), aalpingitia, tubo-overian abecesa				
Outpatient rx limit to pts with temp <38 C WBC <11 000/mm³ minimal evidence of peritonitis active bowel sounds & able to tolerate oral nourishment	N gonorrhoeae chlamydia bacteroides Enterobacteriaceae streptococci	**Outpatient rx:** [(**Oflox** 400 mg po bid or **Levo** 500 mg po qd) + (**metro** 500 mg po bid) x14 d] **OR** [(**ceftriaxone** 250 mg IM or IV x1) (+ **metro** 500 mg po bid x14d) + (**doxy** 100 mg po bid x14 d)]	**Inpatient regimens:** [(**Cefotetan** 2 gm IV q12h or **cefoxitin** 2 gm IV q6h) + (**doxy** 100 mg IV/po q12h)] (**Clinda** 900 mg IV q8h) + (**gentamicin** 2 mg/kg loading dose then 1 5 mg/kg q8h or 4 5 mg/kg 1x/d) then **doxy** 100 mg po bid x14 d	Alternative parenteral regimens 1 (Oflox 400 mg IV q12h or Levo 500 mg IV qd) + metro 500 mg IV q8h 2 AM/SB 3 gm IV q6h + doxy 100 mg IV/po q12h + Levo Remember Evaluate and treat sex partner

† **P Caph 2** (**cetoxitin** 2 0 gm q6–8h IV **cefotetan** 2 0 gm q12h IV **cefuroxima** 750 mg q8h IV) **TC/CL** 3 1 gm q6h IV **AM/SB** 3 0 gm q6h IV **PIP/TZ** 3 375 gm q6h or for nosocomial pneumonia 4 5 gm q6h IV **doxy** 100 mg q12h IV or po **clinda** 450 900 mg q8h IV **APAG** (**gentamicin** *see Table 10C page 72*) **P Ceph 3** (**cefotaxime** 2 0 gm q8h IV **caftriaxone** 2 0 gm qd IV) **ertapenem** 1 0 gm qd IV **IMP** 0 5 gm q6h IV **MER** 1 0 gm q8h IV **azithro** 500 mg IV/d **linazolid** 600 mg IV/po q12h **vanco** 1 0 gm IV q12h

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (16)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT, Women *(continued)*				
Vaginitis—*MMWR 51(RR-6) 2002* or *CID 35 (Suppl 2) S135 2002*				
Candidiasis Pruritus thick cheesy discharge pH <4 5 *See Table 11A, page 76*	Candida albicans 80–90% C glabrata C tropicalis may be increasing– they are less susceptible to azoles	**Oral azoles:** **Fluconazole** 150 mg po x1 **itraconazole** 200 mg po bid x1 day	**Intravaginal azoles** variety of strengths from 1 dose to 7–14 d Drugs available (all end in -azole) butoconazole, clotrimazole, miconazole, tioconazole, terconazole *(doses Table 11A footnote page 76)*	Nystatin vag tabs x14 d less effective Other rx for azole resistant strains gentian violet boric acid If recurrent candidiasis (4 or more episodes/yr) 6 mos suppression with fluconazole 150 mg po q week or itraconazole 100 mg po qd or clotrimazole vag suppositories 500 mg q week
Trichomoniasis Copious foamy discharge, pH >4 5 Treat sexual partners—*see Comment*	Trichomonas vaginalis	**Metro** 2 0 gm as single dose or 500 mg po bid x7 d OR **Tinidazole** 2 0 gm po single dose **Pregnancy** *See Comment*	**For rx failure:** Re-treat with metro 500 mg po bid x7 d , if 2nd failure metro 2 0 gm po qd x3–5 d If still failure suggest ID consultation and/or contact CDC 770-488-4115 or www cdc gov/std	**Treat male sexual partners (2.0 gm metronidazole as single dose).** Nearly 20% men with NGU are infected with trichomonas *(JID 188 465 2003)* Another option if metro resistant **Tinidazole** 500 mg po qid + intravaginal 500 mg po bid x14 d Available from Panorama Pharm 800-247-9767 Ref *CID 33 1341, 2001* **Pregnancy** No data indicating metro teratogenic or mutagenic *[MMWR 51(RR 6) 2002]*
Bacterial vaginosis Malodorous vaginal discharge pH >4 5	Polymicrobic associated with Gardnerella vaginalis bacteroides non-fragilis mobiluncus peptococci Mycoplasma hominis	**Metro** 0 5 gm po bid x7 d or **metro veginal gel**[1] (1 applicator intravaginally) 1x/d x5 d	**Clinda** 0 3 gm bid po x7 d or 2% **clinda vaginal cream** 5 gm intravaginally hs x7 d or **clinda ovules** 100 mg intravaginally hs x3 d	Rx of male sex partner **not** indicated unless balanitis present **Metro 2.0 gm po x1 not as affective as 5–7 day coursa** *(JAMA 268 92 1992)* Metro extended release tabs 750 mg po qd x7 d available no published data **Pregnancy:** Rx same as non-pregnancy except avoid clindamycin cream (↑ risk premature birth) Treatment of asymptomatic pts with oral clinda ↓ premature birth *(Ln 361 983 2003)*
Men:				
Balanitis	Candida 40% Group B strep gardnerella	Oral **azoles** as for vaginitis		Occurs in ¼ of male sex partners of women infected with candida Exclude circinate balanitis (Reiter s syndrome) Plasma cell balanitis (non-infectious) responds to hydrocortisone cream
Epididymo-orchitis				
Age <35 years	N gonorrhoeae Chlamydia trachomatis	**Ceftriaxone** 250 mg IM x1 + **doxy** 100 mg po bid x10 d or **Oflox** 300 mg bid po x10 d		Also bedrest scrotal elevation and analgesics
Age >35 years or homosexual men (insertive partners in anal intercourse)	Enterobacteriaceae (coliforms)	**FQ:** (**CIP-ER** 500 mg po 1x/d or **CIP** 400 mg IV bid or **Levo** 750 mg IV/po 1x/d) x10–14 d	**AM/SB P Caph 3 TC/CL PIP/TZ** *(Dosage see footnote page 16)*	Midstream pyuria and scrotal pain and edema Also bedrest scrotal elevation and analgesics
Prostatitis—Review *AJM 106 327, 1999*				
Acute ≤35 years of age	N gonorrhoeae C trachomatis	**Oflox** 400 mg po x1 then 300 mg po bid x10 d or **ceftriaxone** 250 mg IM x1 then **doxy** 100 mg bid x10 d		Oflox effective vs gonococci & C trachomatis and penetrates prostate In AIDS pts prostate may be focus of Cryptococcus neoformans
≥35 years of age	Enterobacteriaceae (coliforms)	**FQ** *(dosage see Epididymo-orchitis >35 yrs above)* or **TMP/SMX** 1 DS tablet (160 mg TMP) bid po x10–14 d		Treat as acute urinary infection 14 days (not single dose regimen) Some authorities recommend 3–4 week rx *(IDCP 4 325 1995)*
Chronic bacterial	Enterobacteriaceae 80% enterococci 15% P aeruginosa	**FQ** (**CIP** 500 mg bid po x4 wks **Levo** 500 mg q24h po x4 wks—*see Comment*)	**TMP/SMX-DS** 1 tab po bid x1–3 mos	With rx failures consider infected prostatic calculi

[1] 1 applicator contains 5 0 gm of gel with 37 5 mg metronidazole

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (17)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS[a] PRIMARY	SUGGESTED REGIMENS[a] ALTERNATIVE[b]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
GENITAL TRACT, Men/Prostatitis *(continued)*				
Chronic prostatitis/chronic pain syndrome (New NIH classification *JAMA 282 236 1999)*	The most common prostatitis syndrome Etiology is unknown molecular probe data suggest infectious etiology *(Clin Micro Rev 11 604, 1998)*	**α-adrenergic blocking agents are controversial** *(AnIM 133 367, 2000)*		Pt has sx of prostatitis but negative cultures and no cells in prostatic secretions Rev *JAC 46 157, 2000*
HAND *(Bites See Skin)*				
Paronychia				
Nail biting manicuring	Staph aureus anaerobes	**Clinda** 300 mg qid po	**Erythro** 500 mg qid po	Onset usually 2–5 days after trauma No lymphangitis
Contact with oral mucosa—dentists anesthesiologists wrestlers	Herpes simplex (Whitlow)	**Acyclovir** 400 mg tid po x10 days	**Famciclovir** or **valacyclovir** should work *see Comment*	Gram stain and routine culture negative Famciclovir/valacyclovir doses used for primary genital herpes should work, *see Table 14, page 108*
Dishwasher (prolonged water immersion)	Candida sp	**Clotrimazole** (topical)		Avoid immersion of hands in water as much as possible
HEART				
Atherosclerotic coronary artery disease	Chlamydia pneumoniae—under study	New name Chlamydophila pneumoniae Ref *JAMA 290 1459 & 1515 2003*		
Infective endocarditis—Native valve—empirical rx awaiting cultures—No IV illicit drugs	NOTE Diagnostic criteria include evidence of continuous bacteremia (multiple positive blood cultures) new murmur (worsening of old murmur) of valvular insufficiency definite emboli and echocardiographic (transthoracic or transesophageal) evidence of valvular vegetations Reviews *NEJM 345 1318 2001 Ln 363 139 2004*			
Valvular or congenital heart disease including mitral valve prolapse but no modifying circumstances *See Table 15C page 126 for prophylaxis*	Viridans strep 30–40% "other" strep 15–25% enterococci 5–18% staphylococci 20-35%	[(**Pen G** 20 mU qd IV continuous or div q4h) or (**AMP** 12 gm qd IV continuous or div q4h) + (**nafcillin** or **oxacillin** 2 0 gm q4h IV) + **gentamicin** 1 0 mg/kg q8h IM or IV *(see Comment)*]	**Vanco** 15 mg/kg[1] q12h IV (not to exceed 2 gm qd unless serum levels monitored) + **gentamicin** 1 0 mg/kg[1] q8h IM or IV	If patient not acutely ill and not in heart failure we prefer to wait for blood culture results If initial 3 blood cultures neg after 24–48 hrs obtain 2–3 more blood cultures before empiric rx started Natcillin/oxacillin + gentamicin may not be adequate coverage of enterococci hence addition of penicillin G pending cultures When blood cultures + modify regimen from empiric to specific based on organism in vitro susceptibilities clinical experience **Gentamicin** used for synergy peak levels need not exceed 4 μg/ml
Infectivs endocerditis—Native vaive—IV illicit drug usa + svidsnce rt-sided endocarditis —empiric rx	S aureus All others rare	**Vanco** 1 0 gm IV q12h	**Dapto** 6 mg/kg q24h *(not FDA-approved indication 9/04)*	Dapto clinical trials for bacteremia/endocarditis in progress Quinupristin/dalfopristin cidal vs S aureus if both constituents active
Infective endocarditis—Native valve—culture positive (Consensus opinion on rx by organism: *JAMA 274:1706, 1995)*(Review: *NEJM 345:1318, 2001)*(Combination rx: *CID 36:615, 2003)*				
Viridans strep S bovis with **penicillin G MIC ≤0.1 μg/ml**	**Viridans strep, S. bovis**	[(**Pen G** 12–18 mU/d IV continuous or q4h **x2 wks**) PLUS (**gentamicin** IV 1 mg/kg q8h IV **x2 wks**)] **OR** (**Pen G** 12–18 mU/d IV continuous or q4h **x4 wks**) **OR** (**ceftriaxone** 2 0 gm qd IV **x4 wks**)	(**Ceftriaxone** 2 0 gm qd IV + **gentamicin** 1 mg/kg IV q8h both **x2 wks**) If allergy pen G or ceftriax use **vanco** 30 mg/kg/d in 2 div doses to 2 gm/d max unless serum levels measured **x4 wks**	Also effective (ceftriaxone 2 0 gm qd) + (netilmicin[1,2] 4 mg/kg qd) x2 wks *(CID 21 1406, 1995)* Target gent levels peak 3 μg/ml trough <1 μg/ml If very obese pt recommend consultation for dosage adjustment Infuse vanco over ≥1 hr to avoid "red man" syndrome S bovis suggests occult bowel pathology Since relapse rate may be greater in pts ill for >3 mos prior to start of rx the penicillin-gentamicin synergism theoretically may be advantageous in this group
Viridans strep S bovis with **penicillin G MIC >0.1 to <0.5 μg/ml**	**Viridans strep, S. bovis, nutritionally variant streptococci, tolerant strep[2]**	**Pen G** 18 mU/d IV (continuous or q4h) **x4 wks PLUS gentamicin** 1 mg/ kg q8h IV **x2 wks NOTE: Low dose of gentamicin**	**Vanco** 30 mg/kg/d IV in 2 div doses to max 2 gm/d unless serum levels documented **x4 wks**	Can use cefazolin for pen G in pt with allergy that is not IgE mediated (e g anaphylaxis) Alternatively can use vanco *(See Comment above on gent and vanco)*

[1] Assumes estimated creatinine clearance ≥80 ml/min *see Table 17*
[2] Tolerant streptococci = MBC 32-fold greater than MIC

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (18)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS[a] PRIMARY	SUGGESTED REGIMENS[a] ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
HEART/Infective endocarditis—Native valve—culture positive *(continued)*				
For viridans strep or S bovis with **pen G MIC ≥0.5** and enterococci susceptible to AMP/pen G vanco gentamicin NOTE Inf Dis consultation suggested	**"Sueceptible" enterococci, viridane etrep, S. bovie, nutritionelly varient etreptococci** (new names are Abiotrophia sp & Granulicatella sp)	[(**Pen G** 18–30 mu/24h IV continuous or q4h **x4–6 wke**) **PLUS** (**gentamicin** 1–1 5 mg/kg q8h IV **x4–6 wke**)] **OR** (**AMP** 12 gm/d IV continuous or q4h + **gent** as above **x4–6 wke**)	**Venco** 30 mg/kg/d IV in 2 div doses to max of 2 gm/d unless serum levels meas ured **PLUS gentemicin** 1–1 5 mg/kg q8h IV **x4–6 wke NOTE: Low dose of gent**	**4 wke of rx if eymptome <3 moe.; 6 wke of rx if eymptome >3 mos.** Vanco for pen-allergic pts do not use cephalosporins Do **not** give gent once-daily for enterococcal endocarditis Target gent levels peak 3 μg/ml trough <1 μg/ml Vanco target serum levels peak 20–50 μg/ml trough 5–12 μg/ml **NOTE:** Because of ↑ frequency of resistance *(see below)* all enterococci causing endocarditis should be tested in vitro for susceptibility to penicillin β-lactamase production gent susceptibility and vanco susceptibility
Enterococci: MIC streptomycin >2000 μg/ml, MIC gentamicin >500–2000 μg/ml, no resistance to penicillin	**Enterococci, high-level eminoglycoside reeietence**	**Pen G** or **AMP** IV as above **x8–12** wks (approx 50% cure)	If prolonged pen G/AMP fails consider surgical removal of infected valve *See Comment*	10–25% E faecalis and 45–50% E faecium resistant to high gent levels May be sensitive to streptomycin check MIC Case report of success with combination of AMP IMP and vanco *(Scand J Inf Dis 29 628, 1997)*
Enterococci: β-lactamase production test is **positive** and **no** gentamicin resistance	**Enterococci, penicillin resietance**	**AM/SB** 3 0 gm q6h IV **PLUS gentemicin** 1–1 5 mg/kg q8h IV **x4–6 wke. Low dose of gent**	**AM/SB** 3 0 gm IV q6h PLUS **venco** 30 mg/kg/d IV in 2 div doses (check levels if >2 gm) **x4–6 wke**	β-lactamase **not** detected by MIC tests with standard inocula Detection requires testing with the chromogenic cephalosporin nitrocetin **Once-deily gentamicin rx not** efficacious in animal model of E faecalis endocarditis *(JAC 49 437 2002)*
Enterococci: β-lactamase test neg pen G MIC >16 μg/ml no gentamicin resistance	**Enterococci, intrineic pen G/AMP resietence**	**Venco** 30 mg/kg/d IV in 2 div doses (check levels if >2 gm) **PLUS gent** 1–1 5 mg/kg q8h **x4–6 wke** *(see Comment)*		Desired vanco serum levels peak 20–50 μg/ml trough 5–12 μg/ml **Gentamicin** used for synergy, peak levels need not exceed 4 μg/ml
Enterococci: Pen/AMP resistant + high-level gent/strep resistant + vanco resistant usually VRE **Conenltetion euggeeted**	**Enterococci, venco-reeistant, ueueliy E. feecium**	No reliable effective rx Can try quinupristin/ dalfopristin (Synercid) or linezolid—see *Comment, footnote[1] and Table 5*	**Teicoplenin** active against a subset of vanco resistant enterococci Teicoplanin is not available in U S	Synercid activity limited to E faecium and is usually bacteriostatic therefore expect high relapse rate Dose 7 5 mg/kg IV (via central line) q8h **Linezolid** active most enterococci but bacteriostatic Dose 600 mg 2x/d IV or po Linezolid failed in pt with E faecalis endocarditis *(CID 37 e29, 2003)*
Stephylococcel endocerditle Aortic end/or mitrel velve infection—MSSA	**Staph. eureus, methicillin-eeneitive**	**Nefcillin** (**oxecillin**) 2 gm q4h IV **x4–6 wke PLUS gentemicin** 1 0 mg/kg q8h IV **x3–5 d NOTE: Low dose of gent for only 3–5 d.**	[(**Cefazolin** 2 0 gm q8h IV **x4–6 wke**) **PLUS** (**gentemicin** 1 0 mg/kg q8h IV **x3–5 d**)] **Low dose of gent OR Venco** 30 mg/kg/d IV in 2 div doses (check levels if >2 gm/d) **x4–6 wke**	If IgE-mediated penicillin allergy 10% cross reactivity to cephalosporins *(AnIM 141 16 2004)* Cetazolin failures reported *(CID 37 1194 2003)* No definitive data pro or con on once-daily gentamicin for S aureus endocarditis At present favor q8h dosing x3–5 d ↑ recognition of IV catheter-associated S aureus endocarditis May need TEE to detect endocarditis 23% of S aureus bacteremia in association with IV catheter had endocarditis *(CID 115 106 & 115, 1999)*, if TEE neg , may only need 2 wks of therapy
Aortic end//or mitrel velve—MRSA	**Staph. eureus, methicillin-reeietant**	**Venco** 1 0 gm IV q12h x4–6 wks	**Depto** 6 mg/kg IV q24h[NAI] x4–6 wks	**Quinuprietin/delfoprietin** cidal if both components active (both active if S aureus sensitive to erythro in vitro) Other alternatives less desirable because bacteriostatic e g TMP/SMX clinda linezolid
Tricuepid velve infection (ueuelly IVDUe): MSSA ***(MRSA next pege)***	**Steph. eureue, methicillin-eensitive**	**Nefcillin** (**oxecillin**) 2 gm q4h IV **PLUS gentamicin** 1 mg/kg q8h IV **x2 wks NOTE: low dose of gent**	**If penicillin ellergy:** Not clear High failure rate with 2 wks of vanco + gentamicin *(CID 33 120, 2001)* Can try longer duration rx of **venco** ± **RIF (if eensitive)**	**2-week regimen not recommended if meteetetic infection (e.g., osteo) or left-sided endocarditie.** 2 reports of success with **4-week orel** regimen CIP 750 mg bid + RIF 300 mg bid Less than 10% pts had MRSA *(Ln 2 1071 1989 AJM 101 68, 1996)*

[1] Three interesting recent reports (1) Successful rx of vanco-resistant E faecium prosthetic valve endocarditis with Synercid without change in MIC *(CID 25 163, 1997)* (2) resistance to Synercid emerged during therapy of E faecium bacteremia *(CID 24 90 1997)*, and (3) super-infection with E faecalis occurred during Synercid rx of E faecium *(CID 24 91, 1997)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function* **NAi** = *Not FDA-approved indication*

TABLE 1 (19)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[5]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
HEART, Infective endocarditis—Native valve—culture positive/Staphylococcal andocarditis/Tricuapid valve infection *(continued)*				
Methicillin resiatance (MRSA)	**Staph. aureus, methicillin-resistant**	**Vanco** 30 mg/kg/d IV in 2 div doses (check levels if >2 gm/d) **x4–6 wks**	Fails/intoleranf fo vanco can try **daptomycin quinu/dalfo,** or **linezolid**[1]	For MRSA no difference in duration of bacteremia or fever between pts rx with **vanco** or **vanco + RIF** *(AnIM 115 674 1991)* **Daptomycin:** Endocarditis studies in progress **Linezolid** Bacteriostatic
Slow-growing fastidious Gm-neg. bacilli	**HACEK group** *(see Comments) (Mayo Clin Proc 72 532 1997)* Change to HABCEK if add Bartonella	**Ceftriaxone** 2 0 gm qd IV **x4 wks**	**AMP** 12 gm qd (continuous or div q4h) **x4 wks** + **gentamicin** 1 0 mg/kg q8h IV or IM **x4 wks**	**HACEK (acronym for Hemophilus parainfluanzae, H. aphrophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)** H aphrophilus resistant to vanco clinda and methicillin Penicillinase-positive HACEK organisms should be susceptible to AM/SB + genfamicin For hemophilus *see CID 24 1087 1997*
Bartonella apecies (for bacteremia *see page 40—Urban trench fever) AAC 48 1921 2004*	B henselae B quinfana	Optimal rx evolving Retrospective & open prospective trials support **gentamicin** 3 mg/kg IV once daily x14 days + **doxy** 100 mg po bid x4–6 wks		**Dx:** Immunofluorescent antibody titer ≥1 800 blood cultures only occ positive or PCR of tissue from surgery **Surgery:** Over ½ pts require valve surgery relation to cure unclear B quintana transmitted by body lice among homeless asymptomatic colonization of RBCs described *(Ln 360 226, 2002)*
Infactive endocarditie—culture negativa				
Fever valvular disease and ECHO vegetations ± emboli and neg cultures	T whippleii O tever *(see below)* psittacosis brucellosis bartonella *(see above)*, fungi	Emphasis is on diagnosis See specific organism for treatment regimens		For **O fevar** see *CID 33 1347 2001* 4 pts with atebrile culture-neg endocarditis had **T. whippleii** identified by PCR ot resected heart valves *(AnIM 131 112 & 144, 1999)* Whipple s endocarditis *(CID 33 1309, 2001)* TMP/SMX or (tobra + β-lactam)
Infective endocarditis—Prosthetic valve—empiric therapy (culturas pending)				
Early (<2 months posf-op)	S epidermidis S aureus Rarely Enterobacferiaceae diphtheroids fungi	**Vanco** 15 mg/kg q12h IV + **gentamicin** 1 0 mg/kg q8h IV + **RIF** 600 mg po daily		Early surgical consulfafion advised Watch for evidence of heart failure
Late (>2 months posf-op)	S epidermidis virdans strep enterococci S aureus			
Infective endocarditis—Prosthetic valve—positive blood cultures Surgical consultation advised retrospecfive analysis shows ↓ mortality ot pts with S aureus endocarditis if valve replaced during anfibiotic rx *(CID 26 1302 & 1310 1998)* also retrospective study showed ↑ risk of death 2 neuro events in assoc with Coumadin rx *(ArIM 159 473 1999)*	Staph epidermidis	(**Vanco** 15 mg/kg q12h IV + **RIF** 300 mg q8h po) **x6 wks** + **gentamicin** 1 0 mg q8h IV **x14 d**		It S epidermidis is susceptible to natcillin/oxacillin in vitro (nof common) then substitute nafcillin (or oxacillin) for vanco
	Staph aureus	Methicillin sensitive (**Nafcillin** 2 0 gm q4h IV + **RIF** 300 mg q8h po) **x6 wks** + **gentamicin** 1 0 mg/kg q8h IV **x14 d.** Methicillin resistant (**Vanco** 1 0 gm q12h IV + **RIF** 300 mg q8h po) **x6 wks** + **gentamicin** 1 0 mg/kg q8h IV **x14 d.**		
	Viridans strep enterococci	*See infective endocarditis native valve culture positive pages 18–20*		
	Enterobacteriaceae or P aeruginosa	**Aminoglycoside** (**tobra** if P aeruginosa) + (**AP Pen** or **P Ceph 3 AP** or **P Ceph 4**)		In theory could substifufe CIP for APAG but no clinical data
	Candida aspergillus	**Ampho B** ± an **azole** e g fluconazole *(Table 11 page 75)*		High mortality Valve replacement plus antifungal therapy standard therapy but some success with antifungal therapy alone *(CID 22 262 1996)*
Infactive endocarditis—Q fevar *LnID 3 709 2003*	Coxiella burnetii	**Doxy** 100 mg po bid + **hydroxychloroquina** 600 mg/d x1 5–3 yrs		**Dx:** Complement-fix IgG antibody of 1 40 to phase II antigen diagnosfic of acute Q fever IgG C F antibody of 1 200 to phase I antigen diagnostic of chronic Q tever *(LnID 3 709 2003)* Want doxy serum conc >5 μg/ml *(JID 188 1322, 2003)*
Intracardiac-device related intactiona: Pacemaker/defibilla tor, left ventricular assist device	S aureus S epidermidis rarely others	**Davice removal** + **vanco** 1 0 gm IV q12h + **RIF** 300 mg po bid	**Device removal** + **dapto** 6 mg/kg IV q24h[NAI] ± **RIF** *(no data)* 300 mg po bid	**Duration of rx after device removal:** For pocket or subcutaneous infection 10–14 d if lead-assoc endocarditis 4–6 wks depending on organism Refs *Circulation 108 2015 2003 NEJM 350 1422 2004*

[1] **Daptomycin** 6 mg/kg/d IV **Quinupriatin/dalfopriatin** (Synercid) 7 5 mg/kg IV (via central venous line) q8h **Linazolid** 600 mg IV or po q12h

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function* **NAI** *Not FDA approved indication*

TABLE 1 (20)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
HEART *(continued)*				
Pericarditis, purulent—empiric rx Rev *Medicine 82 385, 2003*	Staph aureus, Strep pneumoniae, Group A strep, Enterobacteriaceae	**Vanco + CIP** *(Dosage see footnote[1])*	**Vanco + CFP** *(see footnote[1])*	Drainage required if signs of tamponade. Forced to use empiric vanco due to high prevalence of MRSA
Rheumatic fever with carditis Ref *CID 33 806 2001* *For acute rheumatic fever see page 41, reactive arthritis below*	Post-infectious sequelae of Group A strep infection (usually pharyngitis)	Diuretics, ASA, and usually prednisone 2 mg/kg/d po		Clinical features: Carditis, polyarthritis, chorea, subcutaneous nodules, erythema marginatum. For Jones criteria *Circulation 87 302 1993* *Prophylaxis see page 41*
JOINT—Also see Lyme Disease *page 39*				
Reactive arthritis				
Reiter's syndrome *(See Comment for definition)*	Occurs wks after infection with C. trachomatis, Campylobacter jejuni, Yersinia enterocolitica, Shigella/ Salmonella sp.	Only treatment is non-steroidal anti-inflammatory drugs		Definition: Urethritis, conjunctivitis, arthritis and sometimes uveitis and rash. Arthritis asymmetrical oligoarthritis of ankles, knees, feet, sacroiliitis. Rash: palms and soles—keratoderma blennorrhagia, circinate balanitis of glans penis. HLA-B27 positive predisposes to Reiter's.
Poststreptococcal reactive arthritis *(See Rheumatic fever above)*	Immunologic reaction after strep pharyngitis: (1) arthritis onset in < 10 d., (2) lasts months, (3) unresponsive to ASA	Treat strep pharyngitis and then NSAIDs (prednisone needed in some pts)		A reactive arthritis after a β hemolytic strep infection in absence of sufficient Jones criteria for acute rheumatic fever. Ref *Mayo Clin Proc 75 144, 2000*
Septic arthritis: Treatment requires both adequate drainage of purulent joint fluid and appropriate antimicrobial therapy. There is no need to inject antimicrobials into joints. Empiric therapy after collection of blood and joint fluid for culture, review Gram stain of joint fluid. *For full differential see Ln 351 197 1998*				
Infants <3 months (neonate)	Staph aureus, Enterobacteriaceae, Group B strep, N. gonorrhoeae	(**Nafcillin** or **oxacillin**) + **P Ceph 3** *(Dosage see Table 16, page 131)* *See Comment*	**Nafcillin** or **oxacillin** + **APAG** *See Comment*	Blood cultures frequently positive. Adjacent bone involved in 2/3 pts. Group B strep and gonococci most common community-acquired etiologies. **If MRSA a concern, use vanco in place of nafcillin/oxacillin.**
Children (3 months–14 years)	Staph aureus 27%, S. pyogenes & S. pneumo 14%, H. influenzae 3%, Gm-neg bacilli 6%, other (GC, N. meningitidis) 14%, unknown 36%	**Vanco** + **P Ceph 3** until culture results available *See Table 16 for dosage* Steroids ?—*see Comment*		Marked ↓ in H. influenzae since use of conjugate vaccine. NOTE: Septic arthritis due to salmonella has no association with sickle cell disease, unlike salmonella osteomyelitis. Duration of treatment varies with specific microbial etiology. Short-course steroid: Benefit reported *(PIDJ 22 883 2003)*
Adults *(review Gram stain)* *See page 39 for Lyme Disease*				
Acute monoarticular				
At risk for sexually-transmitted disease	**N. gonorrhoeae** *(see page 15)*, S. aureus, streptococci, rarely aerobic Gm neg. bacilli	**Gram stain negative: Ceftriaxone** 1.0 gm qd IV or **cefotaxime** 1.0 gm q8h IV or **ceftizoxime** 1.0 gm q8h IV	If Gram stain shows Gm+ cocci in clusters **vanco** 1.0 gm q12h IV	For rx comments *see Disseminated GC page 15*
Not at risk for sexually-transmitted disease	S. aureus, streptococci, Gm-neg. bacilli	**All empiric choices guided by Gram stain** **Vanco + P Ceph 3** | **Vanco** + (**CIP** or **Levo**) *For treatment duration see Table 3* *For dosage, see footnote page 23*		Differential includes gout and chondrocalcinosis (pseudogout). **Look for crystals in joint fluid.** Levo has appropriate in vitro spectra and should work, but no clinical data. NOTE: Substitute vanco for nafcillin/oxacillin if MRSA suspected or proven
Chronic monoarticular	Brucella, nocardia, mycobacteria, fungi	*See Tables 2, 11, & 12*		
Polyarticular, usually acute	**Gonococci**, B. burgdorferi, acute rheumatic fever, viruses, e.g., hepatitis B, rubella, vaccine, parvo B19	Gram stain usually negative for GC. If sexually active, culture urethra, cervix, anal canal, throat, blood, joint fluid, and then **ceftriaxone** 1.0 gm IV daily		If GC, usually associated petechiae and/or pustular skin lesions and tenosynovitis. Consider Lyme disease if exposure areas known to harbor infected ticks *See page 39* Expanded differential includes gout, pseudogout, reactive arthritis (HLA-B27 pos.)

[1]**APAG** *(see Table 10C, page 72)* **IMP** 0.5 gm q6h IV, **MER** 1.0 gm q8h IV, **nafcillin** or **oxacillin** 2.0 gm q4h IV, **TC/CL** 3.1 gm q6h IV, **PIP/TZ** 3.375 gm q6h or 4.5 gm q8h IV, **AM/SB** 3.0 gm q6h IV, **P Ceph 1** (**cephalothin** 2.0 gm q4h IV or **cefazolin** 2.0 gm q8h IV), **CIP** 750 mg bid po or 400 mg bid IV, **vanco** 1.0 gm q12h IV, **Rif** 600 mg qd po, **aztreonam** 2.0 gm q8h IV, **CFP** 2.0 gm IV q12h

(Footnotes and abbreviations on page 45) *NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (21)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE‡	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
JOINT *(continued)*				
Septic arthritis, post intra-articular injection	MSSE/MRSE 40%, MSSA/ MRSA 20% P aeruginosa, Propionibacteria	**NO empiric therapy.** Arthroscopy for culture/sensitivity crystals washout		Treat based on culture results x14 days (assumes no foreign body present)
Infected prosthetic joint *CID 36 1157, 2003, JAC 53 127 2004* *See surgical options in Comments*	*See below*	**No empiric therapy.** Need culture & sens results Surgical options in Comment		**Surgical options: 1. 2-stage:** Remove infected prosthesis & leave spacer antimicrobics then new prosthesis Highest cure rate **2. 1-atage:** Remove infected prosthesis debride new prosthesis then antimicrobics **3. Extensiva debridement & leava prosthesis in placa** Antimicrobic therapy Other Remove prosthesis & treat ± bone fusion of joint Last Chronic antimicrobic suppression Value of RIF *JAMA 279 1537 & 1575 1998*
	S pyogenes Gps A B, or G viridans strep	Debridement & prosthesis retention (**Pen G** or **ceftriax**) IV x4 wks Cured 17/19 pts *(CID 36 847, 2003)*		
	MSSE/MSSA	(**Nafcillin/oxecillin** IV + **RIF** po) x6 wks	(**Vanco** IV + **RIF** po) x6 wks	
	MRSE/MRSA	(**Vanco** IV + **RIF** po) x6 wks	[(**CIP** or **Levo**—if susceptible—po) + (**RIF** po)] x6 wks	
	P aeruginosa	**Ceftaz** IV + (**CIP** or **Levo** po)		*AAC 39 2423, 1995*
Rhaumatoid arthritis	TNF inhibitors (adalimumab, etanercept infliximab) ↑ risk of TBc, fungal infection *(CID 38 1261 2004)* Treat latent TBc first *(MMWR 53 683, 2004) See TNF, page 41*			
Saptic bursitis: Olecranon bursitis; prapatellar bursitis	Staph aureus >80%, M tuberculosis (rare) M marinum (rare)	(**Nafcillin** or **oxacillin** 2 gm IV q4h or **dicloxacillin** 500 mg po qid) if MSSA	(**Vanco** 1 gm IV q12h or **linezolid** 600 mg po bid) if MRSA	**Initially aepirata daily and treat for a minimum of 2–3 waeks.** If recurrence surgical excision of bursa—should not be necessary often if treated for 3 weeks + Ref *Semin Arth & Rheum 24 391, 1995*
		Other doses, see footnote page 23		
KIDNEY, BLADDER AND PROSTATE *[For review see AJM 113(Suppl 1A) 1S, 2002 & NEJM 349 259 2003]*				
Acute uncomplicated urinary tract infection (cystitis-urethritis) [NOTE Routine urine culture not necessary self-rx works *(AnIM 135 9, 2001)*] Try to spare FQs *(CID 39 75, 2004)*				
NOTE: Resistance of E. coli to TMP/SMX approx 15–20% *(CID 36 183, 2003)* & correlates with microbiological/ clinical failure *(CID 34 1061 & 1165 2002)* **Racant raports of E. coli resistant to CIP & Levo ae well**	Enterobacteriaceae (E coli) Staph saprophyticus enterococci	Local E coli resistant to TMP/SMX <20% & no allergy **TMP/SMX-DS** bid x3 d if E coli resistant ≥20% or sulfa allergy **NF** x7 d or **fosfomycin** single dose	Local E coli resistant ≥20% or TMP/SMX allergy then 3 days of **CIP** 250 mg bid **CIP-ER** 500 mg qd **Gati** 200 or 400 mg qd **Levo** 250 mg qd **Do not use Moxi or Gemi.**	7-day rx recommended in pregnancy [discontinue or do not use sulfonamides (TMP/SMX) near term (2 weeks before EDC) because of potential ↑ in kernicterus] If failure on 3-day course culture and rx 2 weeks **Fosfomycin** 3 0 gm po x1 less effective vs E coli than multi-dose TMP/SMX or FQ *(Med Lett 39 66 1997)* Fosfo active vs E faecalis poor activity vs other coliforms **Moxifloxacin & gemifloxacin:** Neither approved for UTIs Do not use inadequate urine concentration **Phenazopyridine (Pyridium)**—non-prescription—may relieve dysuna 200 mg po tid x2 d Hemolysis if G6PD deficient
Risk factors for STD Dipstick positive leukocyte esterase or hemoglobin neg Gram stain	C trachomatis	**Doxy** 100 mg bid po x7 d	**Azithro** 1 0 gm single dose po	Pelvic exam for vaginitis & herpes simplex urine LCR/PCR for GC and C trachomatis
Recurrent (3 or more episodes/ year) in young women	Any of the above bacteria	Eradicate infection then TMP/SMX 1 single-strength tab qd po long term		A cost-effective alternative to continuous prophylaxis is self administered single dose rx (TMP/SMX DS 2 tabs 320/1600 mg) at symptom onset Another alternative 1 DS tablet TMP/SMX post-coitus
Child ≤5 yrs old and grade 3–4 reflux	Coliforms	[**TMP/SMX** (2 mg TMP/10 mg SMX)/kg po qd] or (**nitrofurantoin** 2 m[illegible] d **CIP** a[illegible] roved as alternative dru[illegible] ages 1–17 ms		
Recurrent UTI in postmenopausal women *See CID 30 152, 2000*	E coli & other Enterobacteriaceae enterococci S saprophyticus	Treat as for uncomplicated UTI Evaluate for potentially correctable urologic factors—*see Comment* NF more effective than vaginal cream in decreasing frequency but Editors worry about pulmonary fibrosis with long-term NF rx *(CID 36 1362, 2003)*		Definition ≥3 culture + symptomatic UTIs in 1 year or 2 UTIs in 6 months Urologic factors (1) cystocele (2) incontinence (3) ↑ residual urine volume (≥50 ml)

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (22)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
KIDNEY, BLADDER AND PROSTATE *(continued)*				
Acute uncomplicated pyelonephritis (usually women 18–40 yrs temperature >102°F definite costovertebral tenderness) [NOTE Culture of urine and blood indicated prior to therapy Report of hemolytic uremic syndrome as result of toxin-producing E coli UTI *(NEJM 335 635 1996)*]				
Moderately ill (outpatient) **NOTE** Increasing resistance of E coli to *both* TMP/SMX & FQs a concern	Enterobacteriaceae (most likely E coli) enterococci (Gm stain of **uncentrifugad** urine may allow identification of Gm-neg bacilli vs Gm+ cocci)	An **FO** po x7 d **CIP** 500 mg bid or **CIP-ER** 1000 mg qd **Gati** 400 mg qd **Levo** 250 mg qd **Oflox** 400 mg bid	**AM/CL,[1] O Ceph** or **TMP/SMX-DS** Treat for 14 days	In randomized double-blind trial bacteriologic and **clinical success highar for 7 daya of CIP than for 14 daya of TMP/SMX** failures correlated with TMP/SMX in vitro resistance *(JAMA 283 1583, 2000)* Since CIP worked with 7-d rx suspect other FQs effective with 7 d of rx Do not use Moxi or Gemi due to low urine concentrations
Hospitalized	E coli most common enterococci 2nd in frequency	**FO** (IV) or (**AMP** + **gentamicin**) or **P Ceph 3** or **AP Pen** Treat for 14 d	**TC/CL** or **AM/SB** or **PIP/TZ** or **ERTA** Treat for 14 d	Treat IV until pt afebrile 24–48 hrs, then complete 2-wk course with oral drugs *(as Moderately ill, above)* If no clinical improvement in 3 days we recommend imaging On CT if single focal mass-like lesion avg response requires 6 d , if lesions diffuse avg response 13 d *(AJM 93 289 1992)* **If pt hypotensive, prompt imaging (Echo or CT) is recommended to ensure absence of obstructive uropathy.** **NOTE: P Ceph 3 & ertap enem not active va enterococci.**
		Dosages in footnote[1] Do not use P Ceph 3 for suspect or proven enterococcal infection		
Complicated UTI/cethetars Obstruction reflux azotemia transplant Foley catheter-related	Enterobacteriaceae P aeruginosa enterococci	(**AMP** + **gent**) or **PIP/TZ** or **TC/CL** or **IMP** or **MER** x2–3 wks	IV **FO CIP Gati Lavo** x2–3 wks	Rule out obstruction Watch out for enterococci and P aeruginosa—not all listed drugs have predictable activity **CIP-ER** oral dose 1000 mg po qd
		Switch to po **FO** or **TMP/SMX** when possible *For dosages see footnote[1]*		
Asymptomatic bacteriuria				
Preschool children		Base regimen on C&S not empirical		Diagnosis requires ≥10^5 CFU/ml urine of same bacterial species in 2 specimens obtained 3–7 days apart
Pregnancy	Aerobic Gm-neg bacilli & Staph hemolyticus	Screen 1st trimester If positive rx 3 d with **amox NF O Caph TMP/SMX** or **TMP** alone		Screen monthly for recurrence Some authorities treat continuously until delivery (stop TMP/SMX 2 wks before EDC) ↑ resistance of E coli to TMP/SMX
Before and after invasive urologic intervention, e.g., Foley catheter	Aerobic Gm-neg bacilli	Obtain urine culture and then rx 3 d with TMP/SMX DS bid		In one study single dose 2-TMP/SMX DS 80% effective *(AnIM 114 713 1991)* Use of silver alloy Foley catheter may ↓ risk of clinically significant bacteriuria *(AJM 105 236 1998; ArIM 160 3294, 2000)*
Naurogenic bladder		No rx in asymptomatic intermittent catheterization if possible		Ref *AJM 113(1A) 67S, 2002*
Asymptometic, advenced age, male or femele		No rx indicated unless in conjunction with surgery to correct obstructive uropathy, measure residual urine vol in females, prostate exam/PSA in males		
Malacoplakia	E coli	**Bethonechol chloride** + (**CIP** or **TMP/SMX**)		Chronic [illegible]o with abnormal inflammat[illegible] r[illegible]ose *See CID 29 444 1999*
Parinephric abscess				
Associated with staphylococcal bacteremia	Staph aureus	**Nafcillin/oxacillin** or **P Ceph 1** *(Dosage see footnote page 21)* if MSSA	**Vanco** if MRSA	Drainage surgical or image-guided aspiration
Associated with pyelonephritis	Enterobacteriaceae	*See pyelonephritis, complicated UTI above*		Drainage surgical or image-guided aspiration
Prostatitis		*See prostatitis, pages 17–18*		

NOTE: qd = once daily bid = twice daily tid = 3 times a day qid = 4 times a day

† **AM/CL** 875/125 mg q12h or 500/125 mg tid po **aztreonam** 2 0 gm IV q8h **FO (IV)** [**CIP** 400 mg bid **Gati** 400 mg qd **Levo** (250 mg po qd for mild uncomplicated disease 500 mg IV qd for hospital pt)] **cefoxitin** 2 0 gm q8h IV **P Ceph 3** [**cefotaxime** 1 0 gm q12h IV for uncomplicated infections up to 2 0 gm q4h IV for life-threatening infections **ceftriaxone** 1 0–2 0 gm qd IV (use 2 0 gm under age 65)] **AP Pen** (**PIP** 3 0 gm q6h IV) **AM/SB** 3 0 gm q6h IV **TC/CL** 3 1 gm q6h IV **PIP/TZ** 3 375 gm q6h or for nosocomial pneumonia 4 5 gm q6h IV **gentamicin** *(see Table 10C page 72)* **TMP/SMX** 2 0 mg/kg (TMP) q6h IV **P Caph 3 AP** (**ceftazidime** 2 0 gm q8h IV) **P Ceph 4** (**CFP** 2 0 gm q12h IV) **ERTA** 1 0 gm qd IV **IMP** 0 5 gm q6h IV **MER** 1 0 gm q8h IV **Nafcillin** or **oxacillin** 2 0 gm q4h IV For **oral cephalosporin** dosages *see Table 10B page 67* **Dicloxacillin** 500 mg po qid **Metronidazole** 500 mg po qid or 15 mg/kg IV q12h (max 4 gm/day) **Vanco** 1 0 gm IV q12h, **linezolid** 600 mg IV/po q12h

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (23)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LIVER *(for spontaneous bacterial peritonitis, see page 31)*				
Cholangitis		*See Gallbladder, page 10*		
Hepatic abscess	Enterobacteriaceae bacteroides enterococci Entamoeba histolytica Yersinia enterocolitica (rare) *For echinococcus, see Table 13, page 99 For cat-scratch disease (CSD) see pages 30 & 38*	**Metro** + (**P Ceph 3** or **cefoxitin** or **TC/CL** or **PIP/TZ** or **AM/SB** or **FO**) **AMP** + **APAG** + **metro** traditional & effective but AMP resistant Gm-neg bacilli increasing	**Metro** (for amoeba) + either **IMP** or **MER** *(Dosage, see footnote page 23)*	**Serological tests for amabiasis should be done on all patients;** if neg surgical drainage or percutaneous aspiration In pyogenic abscess ½ have identifiable GI source If amoeba serology positive, treat with metro alone without surgery Metro included for both E histolytica & bacteroides **Hemochromatosis** associated with Yersinia enterocolitica liver abscess *(CID 18 938 1994)* regimens listed are effective for yersinia
Leptospirosis	Leptospirosis *see page 40*			
Pallosis hepatis in AIDS pts	Bartonella henselae and B quintana	*See page 38*		
Post-transplant biloma *(CID 39 517, 2004)*	Enterococci (incl VRE) candida Gm-neg bacilli (P aeruginosa 8%) anaerobes 5%	**Linazolid** 600 mg IV bid + **CIP** 400 mg IV q12h + **fluconazole** 400 mg qd IV	**Dapto** 6 mg/kg/d + **Levo** 750 mg IV qd + **fluconazole** 400 mg IV qd	Suspect if fever & abdominal pain post-transplant Exclude hepatic artery thrombosis Presence of candida and/or VRE bad prognosticators
Viral hepatitis	Hepatitis A B C D E G	*See Table 14*		
LUNG/Bronchi				
Bronchiolitis/wheezy bronchitis (expiratory wheezing)				
Infants/children (≤ age 5)	**Respiratory syncytial virus** (RSV) 50% parainfluenza 25% other viruses 20%	Antibiotics not useful mainstay of rx is oxygen Ribavirin of no benefit *(AJRCCM 160 829 1999)* 2 products available for prevention **RSV-immuna globulin** and a humanized mouse monoclonal antibody **palivizumab** *See Table 14 page 112*		RSV most important Rapid dx with antigen detection methods Ribavirin No data on IV ribavirin but little enthusiasm Emphasis now on vaccine development and preventive modulation with immunoglobulins Reviews *PIDJ 19 773 2000 Red Book of Peds 2003, 26th Ed*
Bronchitis				
Infants/children (≤ age 5)	< Age 2 Adenovirus age 2–5 Respiratory syncytial virus parainfluenza 3 virus	Antibiotics indicated only with associated sinusitis or heavy growth on throat culture for S pneumo Group A strep H influenzae or no improvement in 1 week Otherwise rx is symptomatic		
Adolescents and adults with acute tracheobronchitis (Acute bronchitis) Ref *ArIM 162 256 2002 AnIM 134 521 2001*	Usually viral M pneumoniae 5% C pneumoniae 5% *See Persistent cough below*	**Antibiotics not indicated.** Antitussive ± inhaled bronchodilators		Purulent sputum alone not an indication for antibiotic rx Azithro was no better than low-dose vitamin C in a controlled trial *(Ln 359 1648 2002)* Expect cough to last 2 weeks If fever/rigors get chest x-ray M pneumoniae & C pneumoniae ref *LnID 1 334 2001* Rare pt with true C pneumo infection may require 6 wks of clarithro to clear organism *(J Med Micro 52 265, 2003)*
Persistent cough (>14 d.), afebrile during community outbreak: Pertussis (whooping cough) 10–20% adults with cough >14 d have pertussis *(CID 32 1691, 2001)* Rev *LnID 2 744 2002*	Bordetella pertussis & occ Bordetella parapertussis Also consider asthma gastroesophageal reflux post-nasal drip	**Peds doses: Azithro/ clarithro** (dose in footnote[1]) OR **erythro estolate** po 40 mg/kg/d div q8–12h x14 d OR **erythro base** po 40 mg/kg/d div q6h x14 d	**Adult doses: Azithro** po 500 mg day 1 250 mg qd days 2–5 OR **erythro estolate** 500 mg po qid x14 d OR **TMP/SMX-DS** 1 tab po bid x14 d OR (**clarithro** 500 mg po bid or 1 0 gm ER qd x7 d)	**3 stages of illness:** catarrhal (1–2 wks) paroxysmal coughing (2–4 wks) and convalescence (1–2 wks) Treatment may abort or eliminate pertussis in catarrhal stage but does not shorten paroxysmal stage **Diagnosis:** PCR on nasopharyngeal secretions or ↑ pertussis-toxin antibody **Rx aimed at eradication of NP carriage. Azithro** works fastest *(PIDJ 22 847 2003)* Hypertrophic pyloric stenosis reported in infants under 6 wks of age given erythro *(MMWR 48 1117, 1999)*
Prophylaxis of household contacts	**Erythromycin—Children:** 50 mg/kg/d po div in 4 doses **Adults:** 500 mg qid po 14 d **Alternative: clarithro** 7 5 mg/kg po bid x14 d **See footnote[2]**			Recommended by Am Acad Ped Red Book 2003 for all household or close contacts community wide prophylaxis not recommended

[1] Peds doses azithro 10 mg/kg/d day 1 then 5 mg/kg 1x/d x4 d *(PIDJ 22 847 2003)* or clarithro 7 5 mg/kg po twice a day x5–7 d

[2] Compliance with erythro poor due to nausea/vomiting, clarithro costs more but compliance should be better

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (24)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG/Bronchi/Bronchitis *(continued)*				
Acute bacterial exacerbation of chronic bronchitis (ABECB), adults (almost always smokers with COPD) Refs *AnIM 134 595 & 600 2001 NEJM 346 988 2002 AnIM 162 256 2002*	Viruses 20-50% C pneumoniae 5% M pneumoniae <1% role of S pneumo H influenzae & M catarrhalis controversial Tobacco use air pollution contribute	**Severe ABECB** = ↑ dyspnea ↑ sputum viscosity/purulence ↑ sputum volume For severe ABECB (1) consider chest x ray esp if febrile &/or low O sat (2) inhaled anticholinergic bronchodilator (3) oral corticosteroid taper over 2 wks (4) D/C tobacco use (5) non invasive positive pressure ventilation **Role of antimicrobial rx debated even for severe disease For mild or moderate disease, no antimicrobial treatment** or maybe amox doxy TMP/SMX or O Ceph **For severe disease,** AM/CL azithro/ clarithro or O Ceph or telithro or FQs with enhanced activity vs drug resistant S pneumo (Gati Gemi Levo or Moxi) ***Drugs & doses in footnote*[1]. Duration** varies with drug range 3–10 d Limit Gemi to 5 d		
Pneumonia				
Neonatal: Birth to 1 month	**Virus:** CMV, rubella H simplex **Bacteria:** Group B strep listeria coliforms S aureus P aeruginosa **Other:** Chlamydia trachomatis syphilis	**AMP** + **gentamicin** ± **cefotaxime** Add **vanco** if MRSA a concern For chlamydia rx **erythro** 12.5 mg/kg po or IV qid x14 d		Blood cultures indicated Consider C trachomatis if afebrile pneumonia staccato cough IgM > 1.8 rx with erythro or sulfisoxazole If MRSA documented **vanco TMP/SMX** & **linazolid** alternatives **Linezolid** dosage birth to age 11 yrs is **10 mg/kg q8h** Ref *PIDJ 22(Suppl.) S158 2003*
CONSIDER TUBERCULOSIS IN ALL PATIENTS; ISOLATE ALL SUSPECT PATIENTS				
Age 1–3 months *(Adapted from NEJM 346 429 2002)* Pneumonitis syndrome Usually afebrile	C trachomatis RSV parainfluenza virus 3 Bordetella S pneumoniae S aureus (rare)	**Outpatient: po erythro** 10 mg/kg q6h or po **azithro** 10 mg/kg x1 then 5 mg/kg x4 d	**Inpatient: IV afebrile erythro** 10 mg/kg IV q6h or **azithro** 2.5 mg/kg IV q12h *(see Comment)* **If febrile** add **cefotaxime** 200 mg/kg/d div q8h	Pneumonitis syndrome cough tachypnea dyspnea diffuse infiltrates afebrile Usually requires hospital care Reports of hypertrophic pyloric stenosis after erythro under age 6 wks not sure about azithro If lobar pneumonia give AMP 200–300 mg/kg/d for S pneumoniae No empiric coverage for S aureus as it is rare etiology
		For **RSV**, *see bronchiolitis page 24*		
Age 4 months–5 years For RSV see *bronchiolitis page 24, & Table 14* Ref *NEJM 346 429 2002*	RSV, other resp viruses S pneumo H flu, mycoplasma S aureus (rare) M tbc	**Outpatient: Amox** 100 mg/kg/d div q8h **Inpatient (not ICU):** No antibiotic if viral or IV **AMP** 200 mg/kg/d div q6h	**Inpatient (ICU): Cefotaxima** 200 mg/kg/d IV div q8h or **ceftriaxone** 50–75 mg/kg/d IV 1x/d	Common 'other' viruses rhinovirus influenza parainfluenza adenovirus *(PIDJ 19 293 2000)* Often of mild to moderate severity S pneumo non-type B H flu in 4–20% Treat x10–14 d NOTE High frequency of resistance of DRSP to cefuroxime *See footnote[1] footnote 1 page 24, footnote 2 page 26 and Table 5, page 54 for rx of drug-resistant S pneumo*
Age 5 years–15 years, Non-hospitalized, immunocompetent *NEJM 346 429, 2002 PIDJ 21 592, 2002*	Mycoplasma Chlamydophila pneumoniae S pneumoniae Mycobacterium tuberculosis Respiratory viruses mixed e.g., influenza Bacterial/viral infection in 23% *(Ped 113 701, 2004)*	[(**Amox** 100 mg/kg/d) + (**Clerithro** 500 mg po bid or 1 gm ER qd Peds dose 7.5 mg/kg q12h)] **OR** (**azithro** 0.5 gm po x1 then 0.25 gm/d, Peds dose 10 mg/kg/d max of 500 mg po then 5 mg/kg/d max 250 mg)	(**Amox** 100 mg/kg/d) + [**Ooxy** 100 mg po bid (if pt >8 yrs old) or **erythro** 500 mg po 4x/d (Peds dose 10 mg/kg po q6h)] **See *Comment regarding macrolide resistance***	If otherwise healthy and if not concomitant with (or post-) influenza S pneumoniae & S aureus uncommon in this subset suspect S pneumo if sudden onset and large amount of purulent sputum **Macrolide-resistant S. pneumo** an issue Higher prevalence of macrolide-resistant S pneumo in pts <5 yrs old *(JAMA 286 1857, 2001)* Mycoplasma PCR/viral culture usually not done for outpatients **Mycoplasma requires 2–3 wks of rx,** C pneumoniae up to 6 wks *(LnID 1 334 2001 J Med Micro 52 265 2003)* Linezolid approved for peds use for pen-susceptible S pneumo (including bacteremia) & methicillin-sensitive S aureus

NOTE: qd = once daily bid = twice daily tid = 3 times a day qid = 4 times a day

[1] **TMP/SMX** 1 double-strength tab (160 mg TMP) bid po **doxy** 100 mg bid po **amox** 500 mg tid po **AM/CL** 875/125 mg bid or 500/125 mg tid po adult dose of **O Ceph** [**cetaclor** 500 mg q8h or 500 mg CD (extended release) q12h po **cefditoren** 200 mg tabs—2 tabs bid **cefixime**[NUS] 400 mg qd po **catpodoxime proxetil** 200 mg q12h po **cefprozil** 500 mg q12h po **loracarbet** 400 mg q12h po **ceftibuten** 400 mg/d **cafuroxime axetil** 250 or 500 mg q12h po **cefdinir** 300 mg q12h or 600 mg q24h] **azithro** 500 mg po initial dose then 250 mg qd x4 or 500 mg po qd x3 d **clarithro** 500 mg q12h po or **clarithro ER** 1000 mg qd x7 d **dirithromycin** 500 mg qd po **Oflox** 400 mg or **CIP** 750 mg q12h po **Lavo** 500 mg qd po or **Gati** 400 mg qd po **Gaml** 320 mg qd po x5 d **Moxi** 400 mg qd po **Katolide: Telithromycin** 800 mg po qd x5 d
NOTE: CIP and ceftibuten have relatively poor in vitro activity vs S pneumo

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (25)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG/Pneumonia *(continued)*				
Children, hospitalized, immunocompetent—2–18 yrs	S pneumoniae, viruses, mycoplasma. consider S aureus if abscesses or necrotizing	**Ceftriaxone** 50 mg/kg/d IV (to max 2 gm/d) + **azithro** 10 mg/kg/d up to 500 mg IV div q12h. Add anti-staph drug if evidance of lung necrosis		**Alternatives are a problem in children:** If proven S. pneumo resistant to azithro & ceftriaxone (or severe ceftriaxone allergy): IV vanco, linezolid or off-label respiratory FQ. No doxy under age 8. Linezolid reported efficacious in children *(PIDJ 22:677, 2003)*. Ceturoxime failures vs DRSP *(CID 29:462, 1999)*
Adults (over age 18)—See IDSA Guidelines *(CID 37:1405, 2003; Chest 125:1888 & 1913, 2004; AJM 117(3A):39S, 2004)*				
Community-acquired, not hospitalized **Empiric therapy** **Microbiologic diagnosis:** (1) Outpts: No studies. (2) Inpts: (a) cultures of sputum & blood, (b) urine Legionella antigen esp. if in ICU, (c) pneumococcal urine antigen *(JCM 41:2810, 2003)* **Focus of therapy is S. pneumo. % resistant:** ceftriax 2, ceturox 21, doxy 12–23, telithro <1, Gati/Levo/Moxi <1, penicillin 17, amox 4, azithro 28, TMP/SMX 24 In vitro resistance rets: *Trust 7—2003, DMID 49:147, 2004*	Varies with clinical setting **No co-morbidity:** Atypicals—M. pneumoniae, et al.[1] S. pneumo, viral **Co-morbidity:** Alcoholism: S. pneumo, anaerobes, coliforms Bronchiectasis: *see Cystic fibrosis, page 29* COPD: H. influenzae, M. catarrhalis, S. pneumo IVDU: Hematogenous S. aureus Post-CVA aspiration: Oral flora incl. S. pneumo Post-obstruction of bronchi: S. pneumo, anaerobes Post-viral: e.g., influenza	**No co-morbidity:** **Azithro** 0.5 gm po x1, then 0.25 gm/d OR **clarithro** 500 mg po bid or **clarithro-ER** 1.0 gm po qd OR **doxy** 100 mg po bid **OR** if antibiotic within 3 months (**azithro** or **clarithro**) + (**amox** 1.0 gm po tid or high dose **AM/CL**) **Duration of rx:** S. pneumo—Not bacteremic until afebrile 3 days —Bacteremic: 10–14 days reasonable C. pneumoniae—Unclear. Some reports suggest 21 days. Some bronchitis pts required 5–6 wks of clarithro *(J Med Micro 52:265, 2003)* Legionella—10–21 days Necrotizing pneumonia 2° to coliforms, S. aureus, anaerobes: ≥2 weeks	**Co-morbidity present:** **Respiratory FQ** *(see footnote[2])* OR [(**azithro** or **clarithro**) + (high dose **amox**, high dose **AM/CL**, **cefdinir**, **cefpodoxime**, **cefprozil**, or **telithromycin**)] *Doses in footnote[3]*	**Azithro/clarithro:** Pro: appropriate spectrum of action, more in vitro resistance than clinical failure *[CID 34(Suppl 1):S27, 2002]*, qd dosing, better tolerated than erythro Con: Overall S. pneumo resistance in vitro 20–30% [*CID 34(Suppl 1):S4, 2002]*. If pen G resist., S. pneumo up to 50%+ resistance. Breakthrough infections reported *(NEJM 346:630, 2002; CID 35:556, 2002)* **Amoxicillin:** Pro: Active 90–95% S. pneumo at 3–4 gm/d Con: No activity atypicals or β-lactamase + bacteria. Need 3–4 gm/day **AM/CL:** Pro: spectrum includes β-lactamase + H. influenzae, M. catarrhalis, MSSA & Bacteroides sp. Con: No activity atypicals **Cephelosporins**—po: Cefditoren, cefpodoxime, cefprozil, ceturoxime & others—*see footnote[3]* Pro: Active 75–85% S. pneumo & H. influenzae. Ceturoxime least active & higher mortality rate when S. pneumo resistant *(CID 37:230, 2003)* Con: Inactive vs atypical pathogens **Doxycycline:** Pro: Active vs S. pneumo *(DMID 49:147, 2004)* but resistance may be increasing. Active vs H. influenzae, atypicals & bioterrorism agents (anthrax, plague, tularemia) Con: Resistance of S. pneumo 18–20% *(CID 35:633, 2002)*. Sparse clinical data *(ArIM 159:266, 1999; CID 37:870, 2003)* **FQs—Respiratory FQs:** Pro: In vitro & clinically effective vs pen-sensitive & pen-resistant S. pneumo. **NOTE: dose of Levo is 750 mg qd.** QD dosing. Gemi only available po. Con: Geographic pockets of resistance with clinical failure *(NEJM 346:747, 2002)*. Drug-drug interactions *(see Table 22A, page 144)*. Unique reversible rash in young females given Gemi. **Ceftriaxone/cefotaxime:** Pro: Drugs of choice for pen-sens. S. pneumo, active H. influenzae, M. catarrhalis & MSSA Con: Not active atypicals or pneumonia due to bioterrorism pathogens. Add macrolide for atypicals. **Telithromycin:** Pro: Virtually no resistant S. pneumo. Active vs atypical pathogens Con: Only available po. Transient reversible blurry vision due to paralysis of lens accommodation; avoid in myasthenia gravis pts.
Community-acquired, hospitalized—NOT in the ICU **Empiric therapy**	Etiology by co-morbidity & risk factors *as above*	**Ceftriaxone** 2.0 gm IV qd (1.0 gm IV qd > age 65) + **azithro** 500 mg IV qd	**Gati** 400 mg IV qd or **Levo** 750 mg IV qd or **Moxi** 400 mg IV qd	

NOTE: qd = once daily; bid = twice daily; tid = 3 times a day; qid = 4 times a day

[1] Atypical pathogens: Chlamydophila pneumoniae, C. psittaci, Legionella sp., M. pneumoniae, C. burnetii (Q fever). (Q fever ref.: *LnID 3:709, 2003*)

[2] Respiratory FQs with enhanced activity vs S. pneumo with HLR to penicillin: **Gati** 400 mg IV/po qd, **Gemi** 320 mg po qd, **Levo** 750 mg IV/po qd, **Moxi** 400 mg IV/po qd. Ketolide: **telithro** 800 mg po qd

[3] **O Ceph** dosage: **Cefdinir** 300 mg po q12h, **cetditoren pivoxil** 200 mg, 2 tabs po bid, **cefpodoxime proxetil** 200 mg po q12h, **cefprozil** 500 mg po q12h, **high dose amox** 1.0 gm po tid, **high dose AM/CL**—use **AM/CL-ER** 1000/62.5 mg, 2 tabs po bid

(Footnotes and abbreviations on page 45) *NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.*

TABLE 1 (26)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG/Pneumonia/Adults *(continued)*				
Community-acquired, hospitalized—IN ICU Empiric therapy	Severe COPD S pneumo H influ M catarrhalis Legionella Post influenza S aureus Coliforms & P aeruginosa rare unless bronchiectasis *(see below)*	**Aggressive attempts at micro. diagnosis justified:** Culture sputum, blood maybe pleural fluid **Urine antigen tests** for both Legionella & S pneumoniae Empiric therapy must be active vs S pneumo & Legionella		Various studies indicate improved outcome when azithro added to a β-lactam *(CID 36 389 & 1239 2003) ArIM 164 1837, 2001 & 159 2562 1999)* Similar results in prospective study of critically ill pts with pneumococcal bacteremia *(AJRCCM 170 440 2004)* **Ertapenem** could substitute for ceftriaxone but limited clinical experience Need azithro for atypical pathogens Do not use if suspect P aeruginosa
		Geti 400 mg IV qd or **Levo** 750 mg IV qd or **Moxi** 400 mg IV qd	**Ceftriaxone** 2 0 gm IV qd (1 0 gm IV qd > age 65) + **azithro** 500 mg IV qd) or **ERTA** 1 0 gm daily IV + **azithro** 500 mg IV qd *(see Comment)*	
Hospital-acquired—usually with mechanicel vantilation (ampiric therapy) Diagnosis confirmed by quantitative cultures *(see Comment)*	Highly variable depending on clinical setting S pneumo S aureus Legionella coliforms P aeruginosa stenotrophomonas acinetobacter anaerobes all possible	(**IMP** 0 5 gm IV q6h or **MER** 1 0 gm IV q8h) plus if suspect legionella or bioterrorism **respiratory FO (Gati, Levo or Moxi)**	(**Cefepime** or **high-dose PIP/TZ**[1]) + **tobra** Add **resp. FQ** if suspect legionella or bioterrorism	**Dx of ventilator-aasociated pneumonia:** Fever & lung infiltrates often **not** pneumonia *(Chest 106 221 1994)* Quantitative cultures helpful bronchoalveolar lavage (>10^4/ml pos) or protect spec brush (>10^3/ml pos) Ref *AJRCCM 165 867 2002* **Microbial etiology:** No empiric regimen covers all possibilities Regimens listed active majority of **S. pneumo legionella** & **most colitorma** Regimens not active vs MRSA Stenotrophomonas & others *see below Specific rx when culture results known* **Ventilator-associated pneumonia—Prevention:** It possible keep head of bed elevated 30° or more Remove N-G endotracheal tubes as soon as possible It available continuous subglottic suctioning Limit stress ulcer prophylaxis Refs *NEJM 340 627, 1999 CCM 32 1396 2004*
		NOTE *Regimen not active vs MRSA—see* specific rx below *See Comment regarding diagnosis Dosages See footnotes pages 16 23 25 & 26*		
Hospital- or community-acquired, neutropenic pt (<500 neutrophils/mm^3)	Any of organisms listed under community- & hospital-acquired + fungi (aspergillus Candida sp)	*See Hospital-acquired, immediately above* Vanco not included in initial rx unless high suspicion of infected IV access or drug-resistant S pneumo Ampho not used unless still febrile after 3 days or high clinical likelihood *See Comment*		See consensus document on management of febrile neutropenic pt *CID 34 730 2002*
Adults—Selected specific rx when culture results (aputum, blood, pleural fluid, atc.) available. *Also see Table 2, page 47*				
Burkholderia (Pseudomonea) psaudomallei (etiology of melioidosis) Ref *Ln 361 1715, 2003*	Gram-negative	**Initial parenteral rx: Ceftazidima** 40 mg/kg IV q8h or **IMP** 20 mg/kg IV q8h Rx minimum 10 days & improving then po therapy →	**Post-perenteral po rx: Adults** *(see Comment for children)* **Chloro** 10 mg/kg q6h x8 wks **Doxy** 2 mg/kg bid x20 wks **TMP/SMX** 5 mg/kg (TMP component) bid x20 wks	**Children ≤8 yrs old & pregnency:** For oral regimen use **AM/CL-ER** 1000/62 5 2 tabs po bid x20 wks Even with compliance relapse rate is 10%
Haemophilus influenzae	β-lactamase negative	**AMP** IV **amox** po **TMP/SMX azithro/clarithro doxy**		25–35% strains β-lactamase positive ↑ resistance to both TMP/SMX and doxy *See Table 10B page 65 for dosages*
	β-lactamase positive	**AM/CL O Ceph 2/3 P Ceph 3 FO azithro/clarithro, telithro[2]**		
Legionella species	**Hospitalized/immunocompromised**	**Azithro IV** or **Levo IV** or **Gati** or **Moxi** *See Table 10B page 65 for dosages* Treat for 10–21 days		Ref *JAC 51 1119 2003* Best legionella website www.legionella.org Urine antigen detects serogroup 1 94% sens travel assoc Legionella 87% sens CAP & 44% hosp -acquired Legionella *(JCM 41 838 2003)*
Moraxella catarrhalis	93% β-lactamase positive	**AM/CL O Ceph 2/3 P Ceph 2/3 macrolide[3] telithro,[2] FO TMP/SMX Doxy** another option *See Table 10B page 65 for dosages*		

[1] **PIP/TZ** dose 4 5 gm IV q6h
[2] **Telithro** = telithromycin 800 mg po qd
[3] **Macrolide** = azithromycin clarithromycin dirithromycin and erythromycin Dirithromycin serum levels inadequate for bacteremic S pneumo

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (27)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG/Pneumonia/Adults, when cultura resuits avaliable *(continued)*				
Paaudomonas aeruginosa	Often ventilator-associated	**PIP/TZ** 4 5 gm IV q6h + **tobra** 5 mg/kg IV once daily *(see Table 10C page 72)*		
Staphylococcus auraua	Natcillin/oxacillin susceptible	**Nafcillin/oxacillin** 2 0 gm IV q4h	**Vanco** 1 0 gm IV q12h or **linezolid** 600 mg IV q12h	Retrospective analysis of 2 prospective randomized double-blind studies of hospital-acquired MRSA showed enhanced survival with linezolid p 0 03 *(Chest 124 1632, 2003)* efficacy perhaps related to superb linezolid lung concentrations Concern of possible misinterpretation of post hoc subgroup analysis expressed with response of authors *Chest 126 314 2004*
	MRSA	**Vanco** 1 0 gm IV q12h	**Linezolid** 600 mg IV q12h	
Stenotrophomonas maltophilie		**TMP/SMX**	**TC/CL** ± **aztraonam**	In vitro synergy rets *AAC 39 2220 1995 CMR 11 57 1998*
Streptococcus pneumoniaa	Penicilin-susceptible	**AMP** 2 0 gm IV q6h **amox** 1 0 gm po tid **macrolida** *(see footnote 2 page 27)*, **pan G** IV [1] **doxy O Ceph 2 P Caph 2/3, teiithro** 800 mg po qd *See Table 10B page 65 for other dosages*		
	Penicilin-resistant high level	**FOa** with enhanced activity **Gati, Gemi, Levo, Moxi** (IV) **P Ceph 3** (resistance rare) high-dose IV **AMP vanco** IV—*see Table 5 page 54 for more data* If all options not possible (e g , allergy) linezolid active 600 m IV or 12h **Telithro** 800 m po d		
LUNG—Othar				
Anthrax **Inhalation** (applies to oro-pharyngeal & gastrointestinal forms): **Treatment** (Cutaneous *See page 34*) Rets *JAMA 287 2236 2002* & *MMWR 50 909 2001* Clinical experience *JAMA 286 2549 2001* CIP rationale *CID 39 303 2004*	Bacillus anthracis **To report posaible biotarrorism event: 770-488-7100** Plague tularemia *see Table 1B page 46* Chest x-ray mediastinal widening & pleural eftusion *(AnIM 139 337 2003 Ln 364 449 2004)*	**Adults (including pregnancy):** (**CIP** 400 mg IV q12h) or (**doxy** 100 mg IV q12h) **plue** (**clindamycin** 900 mg IV q8h and/or **RiF** 300 mg IV q12h) Switch to po when able & lower CIP to 500 mg po bid clinda to 450 mg po q8h & RIF 300 mg po bid Treat x60 days Other alternatives *Table 2 page 47*	**Childran:** (**CIP** 10 mg/kg IV q12h or 15 mg/kg po q12h) or (**Doxy** >8 y/o & >45 kg 100 mg IV q12h >8 y/o & ≤45 kg 2 2 mg/kg IV q12h ≤8 y/o 2 2 mg/kg IV q12h) **piua clindamycin** 7 5 mg/kg IV q6h **and/or RIF** 20 mg/kg (max 600 mg) IV qd Treat x60 d *See Table 16 page 131 for oral dosage*	1 Clinda may block toxin production 2 Rifampin penetrates CSF & intracellular sites 3 If isolate shown penicillin susceptible a **Adults: Pen G** 4 mU IV q4h b **Children: Pen G** <12 y/o 50 000 U/kg IV q6h >12 y/o 4 mU IV q4h c Constitutive & inducible β-lactamases—do not use pen or amp alone 4 Do not use cephalosporins or TMP/SMX 5 Erythro azithro activity borderline clarithro active 6 No person-to-person spread
Post-exposure **prophylaxia**	Info www bt cdc gov	**Adults (including pregnancy): CIP** 500 mg po bid x60 d **Children: CIP** 20–30 mg/kg/d div q12h x60 d	**Adults (inciuding pregnancy): Doxy** 100 mg po bid x60 d **Children** *(see Comment)* **Doxy** >8 y/o & >45 kg 100 mg po bid >8 y/o & ≤45 kg 2 2 mg/kg po bid ≤8 y/o 2 2 mg/kg po bid All for 60 days	1 Once organism shows suscept to penicillin switch to amoxicillin 80 mg/kg/d div q8h (max 500 mg q8h) pregnant pt to amoxicillin 500 mg po tid 2 Do **not** use cephalosporins or TMP/SMX 3 Other FQs (Gati Levo, Moxi) & clarithro should work but no clinical experience
Aspiration pneumonia ± lung abscaas *(QJM 88 409 1995)*	Bacteroides sp (~15% B fragilis) peptostreptococci Fusobacterium sp S milleri group nocardia (pts taking steroids)	**Clinda** 450–900 mg q8h IV *(For nocardia see Table 11 page 80)*	(**Cefoxitin** 2 0 gm q8h IV) or (**TC/CL** 3 1 gm q6h IV) or (**PIP/TZ** 3 375 gm q6h or 4 5 gm q8h IV) [Historically **pen G** (HD) has been effective]	Bronchoscopy to R/O neoplasm if pt fails to clear or recurs Metro not as effective in putrid lung abscess as clinda Occasionally Type 3 pneumococci Staph aureus Klebsiella pneumoniae are etiologic A recent review questioned the etiologic role of anaerobic bacteria the editors respectfully disagree *(NEJM 344 665 2001)*
Chronic pnaumonia with faver, night swaats and weight loss	M tuberculosis coccidioidomycosis histoplasmosis	*See Tables 11 12*		HIV+ foreign-born alcoholism contact with TB travel into developing countries

[1] **IV Pan G dosage:** Blood cultures neg 1 mU IV q4h blood cultures pos & no meningitis 2 mU IV q4h Another option is continuous infusion (CI) 3 mU loading dose & then CI of 10–12 mU over 12 hrs *(Chest 112 1657 1997)*

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (28)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG/Other *(continued)*				
Cystic fibrosis				
Acute exacerbation of pulmonary symptoms	S aureus or H influenzae early in disease P aeruginosa later in disease	**For P. aeruginosa: Tobra** 3 3 mg/kg q8h or 10 mg/kg IV qd Combine tobra with (**PIP** or **ticarcillin** 100 mg/kg q6h) or with **ceftaz** 50 mg/kg q8h IV *Also see footnote[Y] & Comment*	**For S. aureus: (1) MSSA—oxacillin/natcillin** 2 0 gm IV q4h *(Peds dose Table 16)* **(2) MRSA—venco** 1 0 gm q12h & check serum levels *See Comment*	Additional therapy Clarithro synergistic with tobra vs P aeruginosa *(AAC 46 1105 2002)* + anti inflammatory properties *(Pharmacotherapy 22 227 2002)* Azithro modestly improved FEV_1 pts chronically infected with P aeruginosa *(JAMA 290 1749 2003)* For pharmacokinetics of aminoglycosides in CF *see JAC 50 553 2002* For chronic suppression of P aeruginosa **inhaled phenol-free tobra** 300 mg bid x28 d then no rx x28 d then repeat cycle *(AJRCCM 167 841 2003 NEJM 340 23 1999 Chest 120 107S 2001)*
	Burkholderia (Pseudomonas) cepacia	**TMP/SMX** 5 0 mg/kg (TMP) q6h IV	**Chloro** 15–20 mg/kg IV or q6h po	B cepacia has become a major pathogen Patients develop progressive respiratory failure 62% mortality at 1 year **Fail to respond to APAG** piperacillin & ceftazidime Patients with B cepacia should be isolated from other CF patients **NOTE:** 3- & 4-drug combinations under study in refractory pts *AAC 43 213 1999*
		For other alternatives see Table 2		
Empyema Ref *CID 22 747, 1996* Pleural effusion review *NEJM 346 1971 2002*				
Neonatal	Staph aureus	*See Pneumonia, neonatal page 25*		Drainage indicated
Infants/children (1 month–5 yrs)	Staph aureus Strep pneumoniae H influenzae	*See Pneumonia age 1 month–5 years page 25*		Drainage indicated
Child >5 yrs to ADULT—Diagnostic thoracentesis chest tube for empyemas				
Acute usually parapneumonic	Strep pneumoniae Group A strep	**Cefotaxime** or **ceftriaxone** *(Dosage see footnote 1 page 23)*	**Venco**	Randomized trial showed benefit of intrapleural streptokinase (250 000 units in 100 ml saline with 2 hr dwell qd for up to 7 d *(AJRCCM 170 49 2004)* Urokinase 100 000 IU/d x3 d effective in double-blind study *(AJRCCM 159 37,1999)*
	Staph aureus Check for MRSA	**Natcillin** or **oxacillin**	**Venco**	Gram-pos cocci in clusters
	H influenzae	**P Ceph 3**	**TMP/SMX** or **AM/SB**	Pleomorphic Gm-neg bacilli ↑ resistance to TMP/SMX
Subacute/chronic	Anaerobic strep Strep millen. Bacteroides sp Enterobacteriaceae, M tuberculosis	**Clinda** 450–900 mg q8h IV + **P Ceph 3**	**Cefoxitin** or **IMP** or **TC/CL** or **PIP/TZ** or **AM/SB** *(Dosage see footnote 1 page 23)*	If organisms not seen treat as subacute Drainage R/O tuberculosis or tumor Pleural biopsy with culture for mycobacteria and histology if TBc suspected *(CID 22 747, 1996)*
Human immunodeficiency virus infection (HIV+)				
CO4 T-lymphocytes <200/mm³ or clinical AIDS Dry cough progressive dyspnea & diffuse infiltrate **Prednisone first if suepect pneumocystis (see Comment)**	Pneumocystis carinii most likely also M tbc fungi Kaposi's sarcoma & lymphoma NOTE AIDS pts may develop pneumonia due to DRSP or other pathogens—*see next box below*	*Rx listed here is for* **severe** *pneumocystis see Table 13 page 96 for po regimens for* **mild** *disease* **Prednisone 1et** ***(see Comment),*** **then :** **TMP/SMX** [IV 15 mg/kg/d div q8h (TMP component) or po 2 DS tabs q8h], total of 21 days	(**Clinda** 600 mg q8h IV + **pnmequine** 30 mg qd po) or (**pentemidine isethionate** 4 mg/kg/d IV) x21 d *See Comment*	Diagnostic procedure of choice is sputum induction If negative bronchoscopy Pts with PCP or <200 CD4 cells/mm³ should be on anti-PCP prophylaxis for life **Prednisone 40 mg bid po x5 d, then 40 mg qd po x5 d then 20 mg qd po x11 d. Is indicated with PCP (pO_2 <70 mmHg), should be given at initiation of anti-PCP rx; don't wait until pt's condition deteriorates** *(Table 13 page 96)* If PCP studies negative consider bacterial pneumonia TBc cocci histo crypto Kaposi's sarcoma or lymphoma **Pentemidine not active vs bacterial pathogens.** **NOTE: Pneumocystis resistant to TMP/SMX, albeit rare, does exist.**
CD4 T-lymphocytes normal Acute onset purulent sputum & pulmonary infiltrates ± pleuritic pain **Isolate pt until TBc excluded: Adults**	Strep pneumoniae H influenzae, aerobic Gm-neg bacilli (including P aeruginosa), Legionella rare M tbc	**P Ceph 3** *(Dosages in footnotes on pages 16 & 23)* ± **azithro** Could use **Geti, Levo,** or **Moxi** IV as alternative *(see Comment)*		If Gram stain of sputum shows Gm-neg bacilli options include P Ceph 3 AP TC/CL PIP/TZ IMP, or MER FQs Levo 500 mg po/IV qd, Gati 400 mg IV/po qd, Moxi 400 mg po/IV qd
As above: Children	Same as adult with HIV + lymphoid interstitial pneumonia (LIP)	As for HIV+ adults with pneumonia If diagnosis is LIP rx with steroids		In children with AIDS LIP responsible for 1/3 of pulmonary complications usually >1 yr of age vs PCP which is seen at <1 yr of age Clinically clubbing, hepatosplenomegaly, salivary glands enlarged lake up gallium, lymphocytosis

[1] Other options (Tobra + aztreonam 50 mg/kg q8h IV), (IMP 15–25 mg/kg q6h IV + tobra) **CIP commonly used in children** e g , CIP IV/po + ceftaz IV *(LnID 3 537, 2003)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (29)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
LUNG/Other *(continued)*				
Viral (interstitial) pneumonia suspected *(See Table 14, page 104)*	Consider Adenovirus coronavirus (SARS), hantavirus, influenza metapneumovirus, parainfluenza virus respiratory syncytial virus	**For influenza A or B: oseltamivir** 75 mg po bid x5 d or **zanamivir** 10 mg inhaled bid x5 d Start within 48 hrs of symptom onset	**For influenza A: rimantadine** 100 mg po x2/d or **amantadine** 100 mg po 2x/d	No known efficacious drugs for adenovirus coronavirus (SARS) hantavirus metapneumovirus parainfluenza or RSV Need travel (SARS) & exposure (Hanta) history
LYMPH NODES (approaches below apply to lymphadenitis without an obvious primary source)				
Lymphadenitis, acute				
Generalized	Etiologies EBV early HIV infection, syphilis toxoplasma tularemia, Lyme disease, sarcoid lymphoma, systemic lupus erythematosus and Kikuchi-Fujimoto disease *(CID 39 138, 2004)* Complete history and physical examination followed by appropriate serological tests Treat specific agent(s)			
Regional				
Cervical—*see cat-scratch disease* (CSD), *below*	CSD (B henselae) Grp A strep Staph aureus anaerobes M TBc (scrotula) M avium M scrofulaceum, M malmoense, toxo tularemia			History & physical exam directs evaluation If nodes fluctuant, aspirate and base rx on Gram & acid-fast stains *Review of mycobacterial etiology CID 20 954, 1995* Kikuchi-Fujimoto disease causes fever and benign self-limited adenopathy the etiology is unknown *(AJM 171 401, 1996 CID 39 138, 2004)*
Inguinal				
Sexually transmitted	HSV, chancroid, syphilis LGV			
Not sexually transmitted	GAS, SA, tularemia CSD			
Axillary	GAS SA CSD, tularemia Y pestis sporotrichosis			
Extremity, with associated nodular lymphangitis (For full description *AnIM 118 883, 1993*)	Sporotrichosis leishmania, Nocardia brasiliensis Mycobacterium marinum Mycobacterium chelonae, tularemia		Treatment varies with specific etiology	A distinctive form of lymphangitis characterized by subcutaneous swellings along inflamed lymphatic channels Primary site of skin invasion usually present regional adenopathy variable
Cat-scratch disease—immunocompetent patient Axillary/epitrochlear nodes 46% neck 26% inguinal 17%	Bartonella henselae Reviews *IDC No Amer 12 137, 1998 AAC 48 1921 2004*	**Azithro** dosage—**Adults** (>45 5 kg) 500 mg po x1 then 250 mg/d x4 d **Children** (<45 5 kg) liquid azithro 10 mg/kg x1 then 5 mg/kg/d x4 d Rx is controversial — *see Comment*	No rx resolves in 2–6 mos Needle aspiration relieves pain in suppurative nodes Avoid I&D	**Clinical** Approx 10% nodes suppurate Atypical presentation in <5% pts i e lung nodules liver/spleen lesions Parinaud's oculoglandular syndrome CNS manifestations in 2% of pts (encephalitis peripheral neuropathy retinitis) **Dx** Cat exposure Positive IFA serology Rarely need biopsy **Rx** Only 1 prospective randomized blinded study used azithro with ↑ rapidity of resolution of enlarged lymph nodes *PIDJ 17 447 1998*
MOUTH				
Odontogenic infection including Ludwig's angina Can result in more serious parapharyngeal space infection *(see page 33)*	Oral microflora infection polymicrobial	**Clinda** 300–450 mg q6h po or 600 mg IV q6–8h	(**AM/CL** 875/125 mg bid or 500/125 mg tid po) or **cefotetan** 2 gm IV q12h	Surgical drainage and removal of necrotic tissue essential β-lactamase producing organisms are ↑ in frequency Ref *Canad Dental Assn J 64 508, 1998* Other parenteral alternatives AM/SB PIP/TZ or TC/CL
Buccal cellulitis Children <5 yrs	H influenzae	**Cefuroxime** or **P Ceph 3** *Dosage see Table 16, page 131*	**AM/CL** or **TMP/SMX**	With Hib immunization invasive H influenzae infections have ↓ by 95% Now occurring in infants prior to immunization
Herpetic stomatitis	Herpes simplex virus 1 & 2	*See Table 14*		
Aphthous stomatitis, recurrent HIV-neg	Etiology unknown	Topical steroids (Kenalog in Orabase) may ↓ pain and swelling, if AIDS *see SANFORD GUIDE TO HIV/AIDS THERAPY*		
MUSCLE				
"Gae gangrene" Contaminated traumatic wound Can be spontaneous without trauma *(CID 28 159, 1999)*	Cl perfringens other histotoxic Clostridium sp	(**Clinda** 900 mg q8h IV) + (**pen G** 24 mU/d div q4–6h IV)	**Ceftriaxone** 2 0 gm q12h IV or **erythro** 1 0 gm q6h IV (not by bolus)	Surgical debridement primary rx Hyperbaric oxygen adjunctive efficacy debated consider if debridement not complete or possible *(NEJM 334 1642 1996)* Clinda ↓ toxin production
Pyomyositis	Staph aureus Group A strep (rarely Gm-neg bacilli) variety of anaerobic organisms	(**Nafcillin** or **oxacillin** 2 0 gm q4h IV) or [**P Ceph 1** (**cefazolin** 2 0 gm q8h IV)] if MSSA	**Vanco** 1 0 gm q12h IV if MRSA	Has been common in tropics rare but occurs in temperate zones *(IDCP 7 265 1998)* Follows exercise or muscle injury *see Necrotizing fasciitis* Now seen in HIV/AIDS *(AJM 91 129 1991)* Add clinda or metro if anaerobes suspected, proven *IDCP 8 252 1999*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
PANCREAS—Reviews—*Ln 361 1447, 2003 JAMA 291 2865, 2004*				
Acute alcoholic (without necrosis) (idiopathic) pancreatitis	Not bacterial	None CT-diagnosed		1–9% become infected but prospective studies show no advantage of prophylactic antimicrobials *(Ln 346 652 1995)* Observe for pancreatic abscesses or necrosis which require rx
Pancreatic abscess, infected pseudocyst, post-necrotizing pancreatitis	Enterobacteriaceae enterococci S aureus S epidermidis, anaerobes candida	Need culture of abscess/infected pseudocyst to direct therapy		Can often get specimen by fine-needle aspiration
Antimicrobic prophylaxis necrotizing pancreatitis	As above	Use of antimicrobial prophylaxis remains unclear—*see Comment* If used, suggest IMP		Meta-analysis of 4 random-controlled trials supportive *(Cochrane Database, 2004 (2) CD002941)*, prospective random double-blind trial—**no** benefit *(Gastro 126 997, 2004*
PAROTID GLAND				
"Hot" tender parotid swelling	S aureus oral flora & aerobic Gm-neg bacilli (rare) mumps, rarely enteroviruses/ influenza **Natcillin** or **oxacillin** 2 0 gm IV q4h			Predisposing factors stone(s) in Stensen's duct dehydration Rx depends on ID of specific etiologic organism
"Cold" non-tender parotid swelling	Granulomatous disease (e g mycobacteria fungi sarcoidosis, Sjogren's syndrome) drugs (iodides, et al), diabetes, cirrhosis, tumors			History/lab results may narrow differential may need biopsy for dx
PERITONEUM/PERITONITIS: *Reference—CID 31 997, 2003*				
Primary (apontaneoua bacterial peritonitis, SBP) Rev *CID 27 669, 1998* ESBL ref *CID 28 683 1999* Microbiology *CID 33 1513, 2001*	Enterobacteriaceae 63% S pneumo 15% enterococci 6–10% anaerobes <1%	[**Cetotaxime** 2 0 gm q8h IV (if life-threatening, q4h)] or [**TC/CL** or **PIP/TZ** or **AM/SB**] OR [**ceftriaxone** 2 0 gm q24h IV] or [**ERTA** 1 0 gm IV qd] **If resistant E. coli/ Klebsiella species (ESBL+), then:** (**IMP** or **MER**) or (**FQ: CIP, Levo Gati, Moxi**) *(Dosage in footnote*[1])		One-year **risk of SBP** in pts with ascites and cirrhosis as high as 29% *(Gastro 104 1133 1993)* 30–40% of pts have neg cultures of blood and ascitic fluid % pos cultures ↑ if 10 ml of pt's ascitic fluid added to blood culture bottles **Duration of rx unclear** Suggest 2 wks if blood culture pos One report suggests repeat paracentesis after 48 hrs of cefotaxime If PMNs <250/mm^3 and ascitic fluid sterile, success with 5 days of rx *(AJM 97 169, 1994 Hepatol 5 457 1985)* IV albumin (1 5 gm/kg at dx & 1 gm/kg on day 3) may ↓ frequency of renal impairment (p 0 002) & ↓ hospital mortality (p 0 01) *(NEJM 341 403, 1999)*
Prevention of SBP Cirrhosis & ascites		**TMP/SMX-DS** 1 tab po 5 d/ wk or **CIP** 750 mg po q wk		**TMP/SMX** ↓ peritonitis or spontaneous bacteremia from 27% to 3% *(AnIM 122 595, 1995)* Ref for CIP *Hepatol 22 1171 1995*
Cirrhosis & UGI bleeding		**CIP** 500 mg po bid x7 d Cautious support from recent meta-analysis *Cochrane Database 2002 (2) CD002907*		
Secondary (bowel perforation, ruptured appendix ruptured diverticula) Refs *NEJM 338 1521 1998 & CID 37 997, 2003)*	Enterobacteriaceae Bacteroides sp enterococci P aeruginosa (3–15%)	**Mild-moderate disease—inpatient—parenteral rx:** (e g , focal periappendiceal peritonitis peridiverticular abscess, endomyometritis) **PIP/TZ** 3 375 gm IV q6h or 4 5 gm IV q8h **OR AM/SB** 3 gm IV q6h **OR TC/CL** 3 1 gm IV q6h **OR ERTA** 1 gm IV qd	[(**CIP** 400 mg IV q12h or **Levo** 750 mg IV q24h) + (**metro** 1 0 gm IV q12h)] or (**CFP** 2 0 gm q12h + **metro**) *See Comment*	Must 'cover' both Gm-neg aerobic & Gm-neg anaerobic bacteria **Drugs active only vs anaerobic Gm-neg. bacilli:** clinda, metro **Drugs active only vs aerobic Gm-neg. bacilli:** APAG P Ceph 2/3/4 aztreonam AP Pen CIP Levo **Drugs active vs both aerobic/anaerobic Gm-neg. bacteria:** cefoxitin cefotetan TC/CL PIP/TZ, AM/SB IMP MER Gati Moxi Increasing resistance (R) of Bacteroides species **Cefoxitin** 4–25 **Cefotetan** 17–87 **Clindamycin** 16–44 **% R** Essentially no resistance metro, PIP/TZ *[CID 35(Suppl 1) S126 2000]* **Ertapenam** less active vs P aeruginosa/Acinetobacter species than IMP or MER Based on in vitro activity, could sub **Geti/Moxi** for **CIP/Levo** but insufficient clinical data If absence of ongoing fecal contamination aerobic/anaerobic culture of peritoneal exudate/ abscess of help in guiding specific therapy Less need for aminoglycosides **With severe pen allergy** can "cover" Gm neg. aerobes with CIP or aztreonam **Remember IMP/MER are β-lactams.**
		Severe life-threatening disease—ICU patient. **IMP** 500 mg IV q6h or **MER** 1 gm IV q8h	[**AMP + metro + (CIP** 400 mg IV q12h or **Levo** 750 mg IV q24h)] **OR** [**AMP** 2 gm IV q6h + **metro** 500 mg IV q6h + **APAG** *(see Table 10C, page 72)*]	
		Concomitant surgical management important.		

[1] Parenteral **IV therapy** for peritonitis **TC/CL** 3 1 gm q6h **PIP/TZ** 3 375 gm q6h or 4 5 gm q8h **AM/SB** 3 0 gm q6h **IMP** 0 5 gm q6h **MER** 1 0 gm q8h **FQ** [**CIP** 400 mg q12h **Oflox** 400 mg q12h **Levo** 500 mg qd **Geti** 400 mg qd **Moxi** 400 mg qd] **AMP** 1 0 gm q6h **APAG** *(see Table 10C, page 72)* **cefotetan** 2 0 gm q12h **cefoxitin** 2 0 gm q8h **cefmetazole** 2 0 gm q8–12h **P Ceph 3** (**cefotaxime** 2 0 gm q4–8h, **ceftriaxone** 1–2 gm qd, **ceftizoxime** 2 0 gm q4–8h) **P Ceph 4** (**CFP** 2 0 gm q12h **cefpirome**[NUS] 2 0 gm q12h), **clinda** 450–900 mg q8h, **metro** 1 0 gm loading then 0 5 gm q6h or 1 0 gm q12h **AP Pen** (**ticarcillin** 4 0 gm q6h **PIP** 4 0 gm q6h **aztreonam** 2 0 gm q8h)

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (31)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
PERITONEUM/PERITONITIS *(continued)*				
Asaociatad with chronic ambulatory peritonaal dialysis (defined as >100 WBC/µl >50% PMNs)	Staph aureus (most common) Staph epidermidis P aeruginosa 7% Gm-neg bacilli 11% sterile 20% M fortuitum (rare)	If of moderate severity can rx by adding drug to dialysis fluid—*see Table 17 for dosage* Reasonable empiric combinations **vanco** + **P Ceph 3 AP** or **vanco** + **APAG** If severely ill rx with same drugs IV (adjust dose for renal failure *Table 17*) & via addition to dialysis fluid *Excellent ref Perit Dialysis Int 13 14, 1993*		For diagnosis concentrate several hundred ml of removed dialysis fluid by centrifugation Gram stain concentrate and then inject into aerobic/anaerobic blood culture bottles A positive Gram stain will guide initial therapy If culture shows Staph epidermidis good chance of saving dialysis catheter if multiple Gm-neg bacilli cultured consider bowel perforation and catheter removal
PHARYNX				
Pharyngitis/Tonsillitis—Reviews	*NEJM 344 205, 2001 AnIM 139 113, 2003* Guideline for Group A strep *CID 35 113, 2002*			
Exudative or diffuse erythema *For relationship to acute rheumatic fever, see footnote*[1] Rheumatic fever ref *Ln 349 935, 1997*	Group A C G strep viral infectious mononucleosis *(NEJM 329 156, 1993)*, C diphtheriae A haemolyticum Mycoplasma pneumoniae In adults only 10% pharyngitis due to Group A strep	**Pen V** po x10 d or if compliance unlikely **benzathine pen** IM x1	**Erythro** x10 d or **O Ceph 2** x4–6 d *(CID 38 1526 & 1535, 2004)* or **clinda** or **azithro** x5 d or **clarithro** x10 d or **dirithro** x10 d	**Dx** In children & adults—Rapid strep test or culture (Some debate *JAMA 291 1587, 2004 & 292 167, 2004)* **Pen allergy & macrolide resistance:** No penicillin or cephalosporin-resistant S pyogenes but now **macrolide-raalat. S. pyogenes** Need culture & in vitro susceptibility testing if clinical failure with empiric azithro/clarithro **S. pyogenes Groupe C & G cause pharyngitis but not a riak for post-strep rheumatic fever.** To prevent rheumatic fever eradicate Group A strep Requires 10 d of pen V po 4–6 d of po O Ceph 2 5 d of po azithro 10 d of clarithro In controlled trial better eradication rate with 10 d clarithro (91%) than 5 d azithro (82%)*(CID 32 1798 2001)*
		Up to 35% of isolates resistant to erythro azithro clarithro clinda *(AAC 48 473, 2004)* *See footnote*[2] *for adult and pediatric dosages* Acetaminophen effective for pain relief *(Br J Gen Prac 50 817, 2000)* If macrolide-resistant & pen-allergy Children—Linezolid should work Adults—FQ or telithro		
	Gonococci	**Ceftriaxone** 125 mg IM x1 + (**azithro** or **doxy**) *(see Comment)*	(**CIP** 500 mg po x1) or (**Gati** 400 mg po x1) or (**Oflox** 400 mg po x1) + (**azithro** or **doxy**) *(see Comment)*	Because of risk of concomitant genital C trachomatis add either (azithro 1 0 gm po x1) or (doxy 100 mg po 2x/d x7 d) *See page 15 for more options*
Asymptomatic post-rx carrier	**Group A strep**	**No rx required**		Routine post-rx throat culture not advised
Multiple repeated culture positive episodes *(CID 25 574, 1997)*	Group A strep	**Clinda** or **AM/CL** po	Parenteral **banzathine pen G** ± **RIF** *(see Comment)* *Dosages in footnote*[2]	Small % of pts have recurrent culture-pos Group A strep with symptomatic tonsillo-pharyngitis Hard to tell if true Group A strep infection or active viral infection in carrier of Group A strep Addition of RIF may help 20 mg/kg/d x4 d to max of 300 mg bid *(J Ped 106 481 & 876 1985)*
Whitish plaques HIV+ (thrush)	Candida albicans *(see Table 11, page 76)*			
Vasicular, ulcerative	Coxsackie A9 B1 5 ECHO (multiple types) Enterovirus 71, Herpes simplex 1,2	Antibacterial agents not indicated but for HSV-1,2 **acyclovir** 400 mg tid po x10 d		
Membranous—Diphtheria or Vincent s angina	C diphtheriae	[**Antitoxin** + **arythro** 20–25 mg/kg q12h IV x7–14 d *(JAC 35 717 1995)*] or [**benzyl pan G** 50 000 U/kg/d x5 d, then po **pen VK** 50 mg/kg/d x5 d]		Diphtheria occurs in immunized individuals Antibiotics may ↓ toxin production ↓ spread of organisms Penicillin superior to erythro in randomized trial *(CID 27 845 1998)*
	Vincent s angina (anaerobes/spirochetes)	**Pen G** 4 mU q4h IV	**Clinda** 600 mg q8h IV	May be complicated by F necrophorum bacteremia *see jugular vein phlebitis (Lemierre s), page 33*

[1] Primary rationale for rx is eradication of Group A strep (GAS) and prevention of acute rheumatic fever (ARF) Benzathine penicillin G has been shown in clinical trials to ↓ rate of ARF from 2 8 to 0 2% This was associated with clearance of GAS on pharyngeal cultures *(CID 19 1110, 1994)* Subsequent studies have been based on cultures not actual prevention of ARF Treatment ↓ duration of symptoms

[2] Treatment of Group A strep **All po unless otherwise indicated. PEDIATRIC DOSAGE; Benzathine panicillin** 25 000 u/kg IM to max 1 2 mU **Pen V** 25–50 mg/kg/d div q6h x10 d **AM/CL** 45 mg/kg/d div q12h x10 d **erythro estolata** 20 mg/kg div bid or **succinate** 40 mg/kg/d div bid x10 d **cefuroxime axetil** 20 mg/kg/d div bid for 4–10 d *(PIDJ 14 295 1995)* **cefpodoxime proxetil** 10 mg/kg div bid x10 d **cefdinir** 7 mg/kg q12h x5–10 d or 14 mg/kg q24h x10 d **cefprozil** 15 mg/kg/d div bid x10 d **clarithro** 15 mg/kg/d div bid x10 d **azithro** 12 mg/kg/d x5 d **clinda** 20–30 mg/kg/d div q8h x10 d **ADULT DOSAGE; Benzathina panicillin** 1 2 mU IM x1 **Pan V** 500 mg bid or 250 mg qid x10 d **erythro** dosage varies– with erythro base 500 mg qid x10 d **cefditoren** 200 mg bid x10 d **cefuroxima axatil** 250 mg bid x4 d **cefpodoxime proxetil** 100 mg bid x4 d **cefdinir** 300 mg q12h x5–10 d or 600 mg qd x10 d **cetditoren** 500 mg bid **cefprozil** 500 mg qd x10 d **NOTE:** All **O Ceph 2** drugs approved for 10 d rx of strep pharyngitis increasing number of studies show efficacy of 4–6 d **clarithro** 250 mg bid x10 d **azithro** 500 mg x1 and then 250 mg daily x4 d or 500 mg qd x3 d **dirithromycin** 500 mg qd x10 d

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (uaual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[3]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
PHARYNX *(continued)*				
Epiglottitis				
Children	H influenzae (rare) S pyogenes S pneumoniae S aureus	**Peds dosage: Cefotaxima** 50 mg/kg q8h IV or **ceftriaxona** 50 mg/kg qd IV	**Peda dosage: AM/SB** 100–200 mg/kg/d div q6h or **TMP/ SMX** 8–12 mg TMP comp /kg/d div q12h	Have tracheostomy set at bedside Chloro is effective but potentially less toxic alternative agents available Review (adults) *JAMA 272 1358 1994)*
Adults	Group A strep H influenzae (rare)	**Adult dosaga:** *See footnote[1] for epiglottitis*		
Parapharyngeal space infection	[Spaces include sublingual submandibular submaxillary (Ludwig s angina used loosely for these) lateral pharyngeal retropharyngeal, pretracheal]			
Poor dental hygiene dental extractions foreign bodies (e g toothpicks fish bones)	Polymicrobic Strep sp anaerobes Eikenella corrodens	(**Clinda** 600–900 mg IV q8h) or (**pan G[2]** 24 mU by cont infusion or div q4–6h IV + **mafro** 1 0 gm load and then 0 5 grn q6h IV)	**Cefoxitin** 2 0 gm q8h IV or **clinde** or **TC/CL** or **PIP/TZ** or **AM/SB** *(Dosage, see footnote 1 page 31)*	Close observation of airway 1/3 require intubation MRI or CT to identify abscess if present surgical drainage Metro may be given 1 0 grn q12h IV
Jugular vein aaptic phlabitia (Lamiarra's disease) *(PIDJ 22 921 2003 CID 31 524, 2000)*	Fusobacterium necrophorum in vast majority	**Pen G[2]** 24 mU qd IV by cont infusion or div q4–6h	**Clinda** 600–900 mg q8h IV	Usual rx includes external drainage of lateral pharyngeal space Emboli pulmonary and systemic common Erosion into carotid artery can occur
Laryngitis (hoarseness)/tracheitis	Viral (90%)	Not indicated		
SINUSES, PARANASAL				
Sinusitis, acute; current ferminology: acuta rhinosinusitis				
Obstruction of amua osfia, viral infection, allergena Refs *Otolaryn-Head & Neck Surgery 130 S1 2004 AnIM 134 495 & 498, 2001* For rhinovirus infections (common cold) *see Table 14 page 112* Pediatric Guidelines *Pediatrics 108 798 2001*	Strep pneumoniae 31% H influenzae 21%, M catarrhalis 2% Group A strep 2% anaerobes 6% viruses 15% Staph aureus 4% **By CT acans, sinus mucosa inflamed in 87% of viral URis; only 2% develop becferial rhinosinusitis**	**Reserve antibiotic rx for pta given decongestants/ analgesica for 7 d. who have (1) maxillary/facial pain & (2) purulenf naaal discharge; if aevere illnesa (pain, faver), freat aoonar—uaually requires hospitalization.** **For mild/mod. diaeaaa: Ask if** antibiotics in prior month and/or DRSP prevalence >30% ?? **NO:** **Amox-HD** or **AM/CL-ER** or **cefdinir** or **cefpodoxime** or **cefprozil** or **felithro** (if pen-allergic)	**YES:** **AM/CL-ER** (adults) or resp **FO** (adults) For pen allergy *see Comments* Use AM/CL susp in peds *In general treat x10 days, exceptions in adult and pediatric doses footnote[3] and footnote 2 page 7*	Rx goals (1) Resolve infection (2) prevent complications of bacterial disease e g bacteremia meningitis brain abscess, (3) avoid chronic sinus disease (4) avoid unnecessary antibiotic rx High rate of spontaneous resolution **For pts with pen/cephalosporin allergy, esp. sevare IgE-mediafed allergy, e.g., hives, anaphylaxia, treatmenf opfiona: clarithro, azithro, felithro, TMP/SMX, doxy or FOa. Avoid FQa if under age 18.** ***Dosagas in footnofe 2 page 32.*** If allergy just skin rash po cephalosporin OK Usual rx 10 days In 1 study results of 3 & 10 d of TMP/SMX the same *(JAMA 273 1015 1995)* Watch for pts with fever & fascial erythema ↑ risk of S aureus infection requires IV **nafcillin/oxacillin (antistaphylococcal penicillin, penicillinase-resistant).** In areas with prevalence of DRSP >30% and recent prior antibiotic use consider increasing amoxicillin dose to 3–3 5 grn/d, use extra amox, do not increase AM/CL beyond standard dosage
Clinical failura after 3 daya	As above consider diagnostic tap/aspirate	**Mild/Mod. Disease: AM/CL-ER** OR (**cefpodoxima cefprozil** or **cefdinir**) *Treat 10 days Adult doses in footnote 2 page 32 & Comment*	**Savera Diaeaaa: Gafi, Gemi, Levo, Moxi**	Pts aged 1–18 yrs with **clinical diagnosis** of sinusitis randomized to placebo amox or AM/CL for 14 d **No difference** in multiple measures of efficacy *(Pediatrics 107 619 2001)* Similar study in adults *ArIM 163 1793 2003* Hence without bacteriologic endpoints data are hard to interpret AM/CL ER ref *AJM 117(Suppl 3A) 23S 2004*

[1] **Ceftriaxone** 2 0 gm IV qd **cefotaxime** 2 0 gm q4–8h IV, **AM/SB** 3 0 gm IV q6h **PIP/TZ** 3 375 gm IV q6h **TC/CL** 3 1 gm IV q4–6h, **TMP/SMX** 8–10 mg/kg/d (based on TMP component) div q6h q8h or q12h

[2] **Penicillin** may be given in divided doses q4–8h or by continuous infusion

[3] **Pediafric doses for sinusitis (all oral): AMoxicillin** high dose 90 mg/kg/d div q8h or q12h **AM/CL-ES** (extra strength) pediatric susp 90 mg amox component/kg/d div q12h **azithro** 10 mg/kg x1 then 5 mg/kg/d x3 d **clarithro** 15 mg/kg/d div q12h **cefpodoxima** 10 mg/kg/d (max 400 mg) div q12–24h **cefuroxime axetil** 30 mg/kg/d div q12h **cefdinir** 14 mg/kg/d once daily or divided bid **TMP/SMX** 8–12 mg TMP/40–60 mg SMX/kg/d div q12h
Adult doses for sinusitis (all oral): AM/CL-ER (Augmentin XR) 2000/125 mg bid **amox high-dose (HD)** 1 0 gm tid **clarithro** 500 mg bid or **clarithro ext. release** 1 0 gm qd **doxy** 100 mg bid **reapirafory FOs** (**Gati** 400 mg qd **Gemi** 320 mg qd *(not FDA indication but should work)* **Levo** 750 mg qd **Moxi** 400 mg qd) **O Caph** (**cafdinir** 300 mg q12h or 600 mg qd **cefpodoxime** 200 mg bid **cefprozil** 250–500 mg bid **cefuroxima** 250 mg bid) **TMP/SMX** 1 double-strength (TMP 160 mg) bid (results after 3 & 10 d rx similar) **telithro** 800 mg qd

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (33)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[3]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SINUSES, PARANASAL/Sinusitis, Acute *(continued)*				
Diabetes mellitus with acute ketoacidosis, neutropenia, deferoxamine rx	Rhizopus sp , (mucor) aspergillus	*See Table 11, pages 73 & 80* Ref *NEJM 337 254, 1997*		*See above*
Hospitalized + nasotracheal or nasogastric intubation	Gm-neg bacilli 47% (pseudomonas acinetobacter, E coli common) Gm+ (S aureus) 35%, yeasts 18% Polymicrobial in 80%	Remove nasotracheal tube and if fever persists recommend sinus aspiration for C/S prior to empiric rx **IMP** 0 5 gm q6h IV or **MER** 1 0 gm q8h IV	(**AP Pen**) or (**ceftaz** + **vanco**) or (**CFP** 2 0 gm q12h IV)	After 7 d of nasotracheal or gastric tubes 95% have x-ray "sinusitis" (fluid in sinuses) but on transnasal puncture only 38% culture + *(AJRCCM 150 776, 1994)* For pts requiring mechanical ventilation for ≥1 wk bacterial sinusitis occurs in <10% *(CID 27 851, 1998)* May need fluconazole if yeast on Gram stain of aspirate Review *CID 25 1441, 1997* Epidemiology study *CID 27 463, 1998*
Sinusitis, chronic Adults	Prevotella anaerobic strep & fusobacterium—common anaerobes Strep sp hemophilus P aeruginosa S aureus, & moraxella—aerobes *(CID 35 428, 2002)*	Antibiotics usually not effective	Otolaryngology consultation If acute exacerbation rx as acute	Pathogenesis unclear and may be polyfactorial damage to osthomeatal complex during acute bacterial disease, allergy ± polyps, occult immunodeficiency and/or odontogenic disease (periodontitis in maxillary teeth)
SKIN				
Acne vulgaris *(Med Lett 44 52 2002, Ped Drugs 5 301 2003, Dermatol 206 29, 2003 JAMA 292 726 2004)*				
Comedonal acne "blackheads " 'whiteheads ' earliest form no inflammation	Excessive sebum production & gland obstruction No Propionibacterium acnes	Once daily Topical **tretinoin** (cream 0 025 or 0 05%) or (gel 0 01 or 0 025%)	All once daily Topical **adapalena** 0 1% gel OR **azelaic acid** 20% cream or **tazarotene** 0 1% cream	Goal is prevention ↓ number of new comedones and create an environment unfavorable to P acnes Adapalene causes less irritation than tretinoin Azelaic acid less potent but less irritating than retinoids Expect 40–70% ↓ in comedones in 12 weeks
Mild inflammatory acne small papules or pustules	Proliferation of P acnes + abnormal desquamation of follicular cells	Topical **erythro** 3% + **benzoyl peroxide** 5%, bid	Can substitute **clinde** 1% gel for erythro	Topical metro has anti-inflammatory activity but P acnes not susceptible If tolerable to pt combine topical antimicrobial with a topical retinoid
Inflammatory acne comedones papules & pustules Less common deep nodules (cysts)	Progression of above events	(Topical **erythro** 3% + **benzoyl peroxide** 5% bid) ± oral antibiotic	Oral drugs (**doxy** 100 mg bid) or (**minocycline** 50 mg bid) Others **tetracycline erythro TMP/SMX clinda**	Systemic **isotretinoin** reserved for pts with severe widespread nodular cystic lesions that fail oral antibiotic rx 4–5 mo course of 0 1–1 0 mg/kg/day Aggressive/ violent behavior reported Tetracyclines stain developing teeth Doxy can cause photosensitivity Minocycline side effects urticaria vertigo, pigment deposition in skin or oral mucosa
Acne rosacea	? skin mite Demodex folliculorum	**Azelaic acid gel** bid topical	**Metro** topical cream bid	More pt satisfaction with azelaic acid *[J Am Acad Derm 40(6 Pt 1) 961 1999]*
Anthrax cutaneous inhalation (pulmonary, mediastinal) **To report bioterrorism event: 770-488-7100; For info: www.bt.cdc.gov** Refs *JAMA 281 1735 1999 & MMWR 50 909, 2001*	B anthracis *See Lung page 28 and Table 1B, page 46*	**Adults (including pregnancy): CIP** 500 mg po bid x60 d **Children: CIP** 20–30 mg/ kg/d div q12h po (to max 1 gm/d) x60 d	**Adults (including pregnancy): Doxy** 100 mg po bid x60 d **Children: Doxy** >8 y/o & >45 kg 100 mg po bid >8 y/o & ≤45 kg 2 2 mg/kg po bid ≤8 y/o 2 2 mg/kg po bid All for 60 days	1 If penicillin susceptible then **Adults: Amox** 500 mg po q8h x60 d **Children: Amox** 80 mg/kg/d div q8h (max 500 mg q8h) 2 Usual treatment of cutaneous anthrax is 7–10 d 60 d in setting of bioterrorism with presumed aerosol exposure 3 Other **FQs** (Gati Levo Moxi) should work based on in vitro susceptibility data
Bacillary angiomatosis: For other In immunocompromised (HIV-1 bone marrow transplant) patients *Also see SANFORD GUIDE TO HIV/AIDS THERAPY*	Bartonella infections *see Cat-scratch disease lymphadenitis page 30 and Bartonella, page 38* Bartonella henselae and quintana	**Clarithro** 500 mg bid po or **azithro** 250 mg qd po or **CIP** 500–750 mg bid po *(see Comment)*	**Erythro** 500 mg qid po or **doxy** 100 mg bid po	In immunocompromised pts with severe disease doxy 100 mg po/IV bid + RIF 300 mg po bid reported effective *(IDC No Amer 12 37 1998, Adv PID 11 1 1996)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (34)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SKIN *(continued)*				
Bite. Remember tetanus prophylaxis—*see Table 20 See* **Table 20C for rabiaa prophylaxis**				
Bat raccoon skunk	Strep & staph from skin rabies	**AM/CL** 875/125 mg bid or 500/125 mg tid po	**Doxy** 100 mg bid po	In Americas **antirabies rx indicated** rabies immune globulin + vaccine *(See Table 20C pages 141–142)*
Cat *(Ref NEJM 340 85 & 138, 1999)* Cat scratch disease *page 30*	**Pasteurelle multocida** Staph aureus	**AM/CL** 875/125 mg bid or 500/125 mg tid po	**Cefuroxime axetil** 0 5 gm q12h po or **doxy** 100 mg bid po **Do not use cephalexin**	80% cat bites become infected **P. multocida resistant to dicloxacillin, cephalexin, clinda; many etraine resistant to arythro** (most sensitive to azithro but no clinical data) P multocida infection develops within 24 hrs Observe for osteo myelitis If culture + for only P multocida can switch to pen G IV or pen VK po
Catfish sting	Toxins	*See Comments*		Presents as immediate pain erythema and edema Resembles strep cellulitis May become secondarily infected, AM/CL is reasonable choice for prophylaxis
Dog *(Ref NEJM 340 85 & 138 1999)*	**P. multocida** S aureus, Bacteroides sp Fusobacterium sp , EF 4, Capnocytophaga	**AM/CL** 875/125 mg bid or 500/125 mg tid po	**Clinda** 300 mg qid po + FQ (adults) or **clinda** + **TMP/SMX** (children)	Only 5% dog bites become infected Prophylaxis may be worthwhile *(AnEM 23 535 1994)* Consider antirabies rx, rabies immune globulin + vaccine *(Table 20C)* May transmit blastomycosis Capnocytophaga in splenectomized pts may cause local eschar sepsis with DIC **P. multocida resistant to diclox, cephalexin, clinda and erythro**, sensitive to FQs in vitro *(AAC 43 1475 1999)*
Human For bacteriology, *see CID 37 1481 2003*	Viridans strep 100% Staph epidermidis 53% corynebacterium 41% **Staph. aureus 29%, eikenella 15%**, bacteroides 82% peptostrep 26%	**Early** (not yet infected) **AM/CL** 875/125 mg bid po x5 d **Later** Signs of infection (usually in 3–24 hrs) (**AM/SB** 1 5 gm q6h IV or **cefoxitin** 2 0 gm q8h IV) or (**TC/CL** 3 1 gm q6h IV) or [**PIP/TZ** (3 375 gm q6h or 4 5 gm q8h) IV] Pen allergy **Clinda** + (either **CIP** or **TMP/SMX**)		Cleaning irrigation and debridement most important For clenched fist injuries, x-rays should be obtained Bites inflicted by hospitalized pts consider aerobic Gm-neg bacilli **Eikenella resistant to clinda, nafcillin/oxacillin, metro, P Ceph 1, and arythro; auscaptible to FQs and TMP/SMX.** For in vitro susceptibility to FQs and macrolides *JAC 41 391 1998*
Pig (swine)	Polymicrobic Gm + cocci Gm-neg bacilli, anaerobes Pasteurella sp	**AM/CL** 875/125 mg bid po	**P Caph 3** or **TC/CL** or **AM/SB** or **IMP**	Information limited but infection is common and serious *(Ln 348 888 1996)*
Prairie dog	Monkeypox	*See Table 14A, page 111* No rx recommended		
Primate, non-human	Microbiology ? Herpesvirus simiae	**Acyclovir** *See Table 14B, page 113*		*CID 20 421, 1995*
Rat	Spirillum minus & Streptobacillus moniliformis	**AM/CL** 875/125 mg bid po	**Ooxy**	Antirabies rx not indicated
Seal	Marine mycoplasma	Tetracycline x4 wks		Can take weeks to appear after bite *(Ln 364 448 2004)*
Snake pit viper *(Ref NEJM 347 347, 2002)*	Pseudomonas sp Enterobacteriaceae Staph epidermidis Clostridium sp	Primary therapy is antivenom Penicillin generally used but would not be effective vs organisms isolated Ceftriaxone should be more effective Tetanus rx prophylaxis indicated		
Spider bite: Most necrotic ulcers attributed to spiders are probably due to another cause Remember cutaneous anthrax *(Ln 364 549, 2004)*				
Widow (Latrodectus)	Not infectious	None	May be confused with "acute abdomen " Diazepam or calcium gluconate helpful to control pain muscle spasm Tetanus prophylaxis	
Brown recluse (Loxosceles) (not west of Nebraska)	Not infectious Ref *CID 32 636, 2001*	**Dapsona** 50 mg qd po *(see Comment)*	Most pts do well without systemic rx Dapsone followed by excision at 6 weeks *(AnSurg 202 659, 1985)* reported effective Screen for G6PD deficiency, if positive dapsone contraindicated *Dapsone inhibits PMNs*	
Boils—Furunculosis—Subcutaneous abacesses in drug addicts ("akin poppers"). Carbuncles = multiple connecting furuncles				
Active lesions	Staph aureus, both MSSA & MRSA	Hot packs incision & drainage	Systemic antibiotics do not shorten course, theoretically lower risk of bacteremia	Epidemic of **community-acquired MRSA**, currently susceptible to TMP/SMX, clinda, minocycline & linezolid If erythro-resistant probably clinda-resistant Seems reasonable in pts with large and/or multiple abscesses and/or fever to (1) do culture & sens & (2) start empiric TMP/SMX-DS, 1 bid

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (35)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SKIN/Boils—Furunculosis—Subcutaneous abacesaes in drug addicts *(continued)*				
To lesaan number of recurrences	MSSA & MRSA	Guided by in vitro susceptibilities (**Diclox** 500 mg po qid or **TMP/SMX-OS** 1 tab po bid) + **RIF** 600 mg po qd all x10 d	**Plus** Nasal & under finger nail treatment with either **bacitracin ointmant** or **mupirocin ointment** bid	Plus Shower with Hibiclens daily x3 d & then 3x/week Others have tried 5% povidone-iodine cream intranasal 4x/d x5 d Reports of S aureus resistant to bacitracin & mupirocin Mupirocin prophylaxis of non-surgical hosp pts had no effect on S aureus infection in placebo-controlled study *(AnIM 140 419 & 484 2004)*
Hidradanitis suppurativa	Lesions secondarily infected S aureus Enterobacteriaceae pseudomonas anaerobes	Aspirate base rx on culture	Many pts ultimately require surgical excision	Caused by keratinous plugging of apocrine glands of axillary and/or inguinal areas
Burns. For overall management *NEJM 350 810 2004*				
Initial burn wound care *(CID 37 543 2003)*	Not infected	Early excision & wound closure shower hydrotherapy Role of topical antimicrobics unclear	**Silver sulfadiazine** cream 1% apply 1–2x/ day or 0 5% **silver nitrate** solution or **mafenide acatata** cream Apply 2x/day	Marrow-induced neutropenia can occur during 1st wk of sulfadiazine but resolves even if use is continued Silver nitrate leaches electrolytes from wounds & stains everything Mafenide inhibits carbonic anhydrase and can cause metabolic acidosis
Burn wound sapsis Variety of skin grafts and skin substitutes *see JAMA 283 717 2000*	Strep pyogenes Enterobacter sp S aureus S epidermidis E faecalis E coli P aeruginosa Fungi rare Herpesvirus rare	(**Vanco** 1 0 gm q12h IV) + (**amikacin** 10 mg/kg loading dose then 7 5 mg/kg q12h IV) + [**PIP** 4 0 gm q4h IV (give ½ daily dose of **piparacillin** into subeschar tissues with surgical eschar removal within 12 hours)]		Monitor serum levels t/2 of most antibiotics ↓ Staph aureus tend to remain localized to burn wound If patient more toxic than expected consider toxic shock syndrome Candida sp colonize but seldom invade Pneumonia has become the major infectious complication most often staph Other infectious complications include septic thrombophlebitis
Cellulitis, erysipelas: Be wary of macrolide (erythro)-resistant) S pyogenes Review *NEJM 350 904, 2004*				
Extremities not associated with venous catheter *(see Comments)* non-diabetic *For diabetes see below*	Group A strep, occ Group B C G Staph aureus (uncommon but difficult to exclude)	**Pen G** 1–2 mU IV q6h or (**Nefcillin** or **oxacillin** 2 0 gm q4h IV) If not severe **dicloxacillin** 500 mg q6h po or **cefazolin** 1 0 gm q8h IV *See Comment*	**Erythro** or **P Ceph 1** or **AM/CL** or **azithro** or **clarithro** or **dirithro** *(Dosage, see footnote page 25)* *See Comment*	**"Spontaneous" erysipelas of leg in non-diabetic is usually due to strep, Gps A,B,C or G.** Hence OK to **start with IV pen G 1–2 mU q6h** & observe for localized S aureus infection Look for tinea pedis with fissures a common portal of entry can often culture strep from between toes *(CID 23 1162, 1996)* For rx of pts with lymphedema & recurrent erysipelas *see prophylaxis Table 15* Other alternatives clinda Gati Levo Moxi
Facial, adult (erysipelas)	Group A strep Staph aureus (to include MRSA) S pneumo	**Vanco** 1 0 gm IV q12h	**Dapto** 4 mg/kg/d	**Choice of ampiric therapy must have activity vs S. aureus** S aureus erysipelas of face can mimic S pyogenes erysipelas of an extremity Forced to treat empirically for MRSA until in vitro susceptibilities available
Diabetes mellitus and erysipelas *(See Foot "Diabetic", page 10)*	Group A strep Staph aureus Enterobacteriaceae clostridia (rare)	**Early mild: TMP/SMX-DS** bid po + **RIF** 300 mg bid po **For severe disease: IMP** or **MER** or **ERTA** IV + **(linezolid** 600 mg bid IV/po or **vanco** IV) *Dosage see page 10, Diabetic foot*		Prompt surgical debridement indicated to rule out necrotizing fasciitis and to obtain cultures If septic consider x-ray of extremity to demonstrate gas **Prognosis dependent on blood supply: asasas arteries.** *See diabetic foot page 10*
Erysipelas 2° to lymphedema (congenital = Milroy's disease); post-breast surgery with lymph node dissection	S pyogenes Groups A C G	**Benzathine pen G** 1 2 mU IM q4 wks [of minimal benefit in reducing recurrences in pts with underlying predisposing conditions *(CID 25 685 1997)*]		Indicated only if pt is having frequent episodes of cellulitis Pen V 250 mg po bid should be effective but not aware of clinical trials In pen-allergic pts erythro 500 mg po qd azithro 250 mg po qd or clarithro 500 mg po qd
Dandruff (saborrheic dermatitis)	Malassezia species	**Ketoconazole shampoo** 2% or **selenium sulfide** 2 5% *(see page 6, chronic external otitis)*		
Decubitus or venous stasis or arterial insufficiency ulcers: with sepsis	Polymicrobic S pyogenes (Gps A C G) enterococci anaerobic strep Enterobacteriaceae Pseudomonas sp Bacteroides sp Staph aureus	**IMP** or **MER** or **TC/CL** or **PIP/TZ** or **ERTA**	(**CIP Gati Levo,** or **Moxi**) + (**clinda** or **matro**) *Dosages see footnotes pages 10, 16 21 42*	Without sepsis or extensive cellulitis local care may be adequate Debride as needed Topical mafenide or silver sulfadiazine adjunctive R/O underlying osteomyelitis May need wound coverage with skin graft or skin substitute *(JAMA 283 716 2000)*
Erythema multiforme	H simplex type 1 mycoplasma Strep pyogenes drugs (sulfonamides, phenytoin penicillins)			**Rx Acyclovir** if due to H simplex

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (36)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SKIN *(continued)*				
Erythema nodosum	Sarcoidosis, inflammatory bowel disease, M. tbc, coccidioidomycosis, yersinia, sulfonamides			**Rx: NSAIDs; glucocorticoids** if refractory
Erythrasma	Corynebacterium minutissimum	**Erythro** 250 mg q6h po x14 d		Coral red fluorescence with Wood's lamp. Alt: 2% aqueous clinda topically
Folliculitis	Many etiologies: S. aureus, candida, P. aeruginosa, malassezia, demodex	*See individual entities. See Whirlpool folliculitis, page 38*		
Furunculosis	Staph. aureus	*See Boils, page 36*		
Hemorrhagic bullous lesions				
Hx of sea water-contaminated abrasion or eating raw seafood + shock	Vibrio vulnificus, V. damsela *(CID 37:272, 2003)*	**Ceftazidime** 2.0 gm q8h IV + **doxy** 100 mg bid (IV or po)	Either **cefotaxime** 2.0 gm q8h IV or (**CIP** 750 mg bid po or 400 mg bid IV)	¾ pts have chronic liver disease with mortality in 50% *(NEJM 312:343, 1985)*. In Taiwan, where a number of cases are seen, the impression exists that ceftazidime is superior to tetracyclines *(CID 15:271, 1992)*, hence both
Herpes zoster/shingles	*See Table 14*			
Impetigo, ecthyma—usually children				
Honey-crust lesions (non-bullous)	**Group A strep impetigo**: crusted lesions can be Staph. aureus + strepto-cocci	Mupirocin ointment 2% tid x3–5 d *For dosages, see Table 10B for adults and Table 16, page 131 for children*	**Azithro** or **clarithro** or **erythro** or **O Ceph 2**	In meta-analysis that combined strep & staph impetigo, mupirocin had higher cure rates than placebo. Mupirocin superior to oral erythro. Penicillin inferior to erythro. Few placebo-controlled trials. Ref: *Cochrane Database Systemic Reviews 2004 (2)*
Bullous (if ruptured, thin "varnish-like" crust)	**Staph. aureus impetigo**	**Dicloxacillin** po or **oxacillin** po or **O Ceph 1**	**Mupirocin** ointment or **AM/CL** or **ezithro** or **clarithro** *For dosages, see Table 10B*	
Infected wound, extremity—Post-trauma *(for bites, see page 35; for post-operative, see below)*—**Gram stain negative**				
Mild to moderate uncomplicated	Polymicrobic: Staph. aureus (MSSA & MRSA), Group A & anaerobic strep, Enterobacteriaceae, Cl. perfringens, Cl. tetani if water exposure, Pseudomonas sp., Aeromonas sp.	**TMP/SMX-OS** po bid or **clinda** 300–450 mg po tid *(see Comment)*	**Minocycline** 100 mg po bid or **linezolid** 600 mg po bid *(see Comment)*	**Cultura & sensitivity, check Gram stain. Tetanus toxoid if indicated.** **Mild infection:** Suggested drugs focus on S. aureus & Strep species. If suspect Gm-neg. bacilli, add **AM/CL-ER** 1000/62.5 two tabs po bid. If MRSA erythro-resistant, may have inducible resistance to clinda. **Fever—sepsis**: Alternative to vanco is **linezolid** 600 mg IV/po q12h. If Gm-neg. bacilli & severe pen allergy: CIP 400 mg IV q12h or Levo 750 mg IV qd.
Febrile with sepsis—hospitalized		[**AM/SB** or **TC/CL** or **PIP/TZ** or **IMP** or **MER** or **ERTA** *(Dosage, page 16)*] + **vanco** 1.0 gm IV q12h	**Vanco** 1.0 gm IV q12h *(see Comment)* + (**CIP** or **Levo** IV)	
Infected wound, post-operative—Gram stain negative				
Surgery not involving GI or female genital tract				
Without sepsis (mild)	Staph. aureus, Group A, B, C or G strep	**TMP/SMX-DS** po bid **Vanco** 1.0 gm IV q12h	**Clinda** 300–450 mg po tid **Dapto** 6 mg/kg IV qd	Check Gram stain of exudate. If Gm-neg. bacilli **add** β-lactam/β-lactamase inhibitor: AM/CL-ER po or (ERTA or PIP/TZ or TC/CL) IV. *Dosage on page 16*
With sepsis (severe)				
Surgery involving GI tract (includes oropharynx, esophagus) or female genital tract	MSSA/MRSA, coliforms, bacteroides & other anaerobes	[**PIP/TZ** or (**P Ceph 3** + **metro**) or **ERTA** or **IMP** or **MER**] + **vanco** 1.0 gm IV q12h **if severely ill.** **Mild infection: AM/CL-ER** 2 tabs po bid Add **TMP/SMX-DS** po bid if Gm+ cocci on Gram stain		For all treatment options, *see Peritonitis, page 31* Most important: Drain wound & get cultures Can sub linezolid for vanco. Can sub CIP or Levo for β-lactams
Meleney's synergistic gangrene	*See Necrotizing fasciitis, page 38*			
Infected wound, febrile patient—Gram stain: Gram-positive cocci in clusters	S. aureus, possibly MRSA	**Do culture & sensitivity** **Oral: TMP/SMX-DS** 1 tab po bid or **clinda** 300–450 mg po tid *(see Comment)*	**IV: Vanco** 1.0 gm IV q12h or **daptomycin** 4 mg/kg IV qd or 6 mg/kg qd if septic	↑ in community-acquired MRSA (CA-MRSA). Need culture & sensitivity to verify. Other po options for CA-MRSA include minocycline 100 mg po q12h (inexpensive) & linezolid 600 mg po q12h (expensive). If MRSA clinda-sensitive but erythro-resistant, watch out for inducible clinda resistance.

(Footnotes and abbreviations on page 45)

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 1 (37)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE‡	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SKIN *(continued)*				
Necrotizing fasciitis ("flesh-eating bacteria")				
Post-surgery trauma strepto coccal skin infections *See Gas gangrene, page 30 & Toxic shock, page 43*	**3 types:** (1) Streptococci Grp A C G (2) Clostridia sp (3) polymicrobic aerobic + anaerobic (if S aureus + anaerobic strep = Meleney s synergistic gangrene)	*For treatment of clostridia, see Muscle, gas gangrene, page 30* The terminology of **polymicrobic** wound infections is not precise Meleney s synergistic gangrene, Fournier s gangrene, necrotizing fasciitis have a common pathophysiology **All require prompt surgical debridement** as well as antibiotics Dx of necrotizing fasciitis requires incision and probing If no resistance to probing subcutaneously (fascial plane) dx = necrotizing fasciitis **Need Gram stain/culture** to determine if etiology is strep clostridia or polymicrobial **Treatment: Pen G** if strep or clostridia **IMP** or **MER** if polymicrobial **NOTE:** If strep necrotizing fasciitis reasonable to treat with penicillin & clinda *(SMJ 96 968, 2003)* if clostridia ± gas gangrene add clinda to penicillin *(see page 30)*		
Puncture wound—nail	Through tennis shoe P aeruginosa	Local debridement to remove foreign body & tetanus prophylaxis		Osteomyelitis evolves in only 1–2% of plantar puncture wounds
Staphylococcal scalded skin syndrome Ref *PIDJ 19 819, 2000*	Toxin-producing S aureus	**Nafcillin** or **oxacillin** 2 0 gm IV q4h (children 150 mg/kg/d div q6h) x5–7 days		Toxin causes **intraepidermal split** and positive Nikolsky sign Drugs cause epiderm/dermal split **called toxic epidermal necrolysis—**more serious *(Ln 351 1417 1998)* Biopsy differentiates
Ulcerated skin lesions	Consider anthrax tularemia P aeruginosa (ecthyma gangrenosum) plague blastomycosis spider (rarely) mucormycosis mycobacteria leishmania arterial insufficiency, venous stasis, and others			
Whirlpool (Hot Tub) folliculitis *See Folliculitis page 37*	Pseudomonas aeruginosa	Usually self limited, treatment not indicated		Decontaminate hot tub drain and chlorinate Also associated with exfoliative beauty aids (loofah s, sponges) *J Clin Micro 31 480, 1993*
SPLEEN. For post-splenectomy prophylaxis, see *Table 15A, page 123*				
Splenic abscess				
Endocarditis, bacteremia	Staph aureus streptococci	**Nafcillin** or **oxacillin** 2 0 gm q4h IV	**Vanco** 1 0 gm q12h IV	Burkholderia (Pseudomonas) pseudomallei is common cause of splenic abscess in SE Asia
Contiguous from intra-abdominal site	Polymicrobic	*Treat as Peritonitis, secondary, page 31*		
Immunocompromised	Candida sp	**Amphotericin B** *(Dosage see Table 11, page 74)*	**Fluconazole, caspofungin**	
SYSTEMIC FEBRILE SYNDROMES				
Spread by infected **TICK, FLEA, or LICE** *(CID 29 888 1999)* Epidemiologic history crucial **Babesiosis, Lyme disease, & granulocytic Ehrlichiosis** have same reservoir & tick vector *(CID 33 676 2001)*				
Babesiosis: see *NEJM 343 1454 2000* Do not treat if asymptomatic young has spleen and immunocompetent	Etiol B microti et al Vector Usually Ixodes ticks Host White-footed mouse & others	[(**Atovaquone** 750 mg po q12h) + (**azithro** 500 mg po day 1 then 250 mg/d) x7 d] OR [**clinda** 1 2 gm bid IV or 600 mg tid po x7 d + **quinine** 650 mg tid po x7 d **Ped. dosage: Clinda** 20–40 mg/kg/d and **quinine** 25 mg/kg/d] plus **exchange transfusion**		Exposure endemic areas May to Sept Can result from blood transfusion *(JAMA 281 927, 1999)* Usually subclinical Illness likely in asplenic pts pts with concomitant Lyme disease older pts pts with HIV Dx Giemsa-stained blood smear antibody test available PCR under study **Rx: Exchange transfusions successful adjunct, used early, in severe disease.**
Bartonella infections: *NEJM 340 184 1999 CID 35 684 2002*				
Asymptomatic bacteremia	B quintana	**Doxy** 100 mg po/IV x15 d		Can lead to endocarditis &/or trench fever found in homeless esp if lice/leg pain
Cat-scratch disease	B henselae	**Azithro** or symptomatic only—*see page 30* usually lymphadenitis, can involve CNS, liver in immunocompetent pts		
Bacillary angiomatosis; Peliosis hepatis—pts with AIDS	B henselae B quintana	(**Clarithro** 500 mg bid or **clarithro ER** 1 0 gm qd po or **azithro** 250 mg qd po or **CIP** 500–750 mg bid, po) x8 wks	(**Erythro** 500 mg qid po or **doxy** 100 mg bid po) x8 wks or if severe combination of **doxy** 100 mg po/IV bid + **RIF** 300 mg po bid *(IDC No Amer 12 137, 1998)*	**Manifestations of Bartonella infections:** **HIV/AIDS Patient:** Bacillary angiomatosis; Bacillary peliosis; Bacteremia/endocarditis/FUO **Immunocompetent Patient:** Bacteremia/endocarditis/FUO; Cat scratch disease; Trench fever
Endocarditis *(see page 20) (AAC 47 2204 2003)*	B henselae B quintana	**Gentamicin** 3 mg/kg IV once daily x minimum 14 d + **doxy** 200 mg po once daily x4–6 wks		Hard to detect with automated blood culture systems Need lysis-centrifugation and/or blind subculture onto chocolate agar at 7 & 14 days Diagnosis often by antibody titer ≥1 800
Trench fever (FUO)	B quintana	**Doxy** 100 mg bid po (doxy alone if **no** endocarditis)		Same as Urban Trench Fever *(page 40)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (38)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC FEBRILE SYNDROMES Spread by infected **TICK, FLEA or LICE** *(continued)*				
Ehrlichiosis[1]. CDC def of confirmed case as one of (1) 4x ↑ IFA antibody (2) detection of Ehrlichia DNA by PCR (3) visible morulae in WBC and IFA ≥1 64 *[MMWR 46(RR-10) 1–55, 1997]*				
Human monocytic ehrlichiosis (HEM) *(IDCP 7 252 1998)*	Ehrlichia chaffeensis (Lone Star tick is vector)	**Ooxy** 100 mg bid po or IV x7–14 d	**Tetracycline** 500 mg qid po x7 14 d No current recommendation for children or pregnancy	30 states mostly SE of line from NJ to Ill to Missouri to Oklahoma to Texas History of outdoor activity and tick exposure April-Sept Fever rash (36%) leukopenia and thrombocytopenia Blood smears no help PCR for early dx
Human granulocytic ehrlichiosis (HGE) *(CID 31 554 2000)*	Anaplasma (Ehrlichia) phagocytophilum (Ixodes sp ticks are vector) Dog variant is Ehrlichia ewingii *(NEJM 341 148 & 195, 1999)*	**Doxy** 100 mg bid po or IV x7–14 d	**Tetracycline** 500 mg 4x/d po x7–14 d Not in children or pregnancy *See Comment*	Upper Midwest NE West Coast & Europe H/O tick exposure April-Sept Febrile flu-like illness after outdoor activity No rash Leukopenia/thrombocytopenia common **Dx:** Up to 80% have positive blood smear Antibody test for confirmation **Rx:** RIF successful in pregnancy *(CID 27 213 1998)* but worry about resistance developing Based on in vitro studies, no clear alternative rx—Levo activity marginal *(AAC 47 413, 2003)*
Lyme Disease NOTE Think about concomitant tick borne disease—babesiosis *(JAMA 275 1657 1996)* or ehrlichiosis Reviews *Lnfd 3 489 & 761 2003 Ln 362 1639 2003*				
Tick bite possible Ixodes acquired in endemic area	Borrelia burgdorferi Urine antigen test reported unreliable *(AJM 110 217 & 236 2001)* Terminology ref *AnIM 136 413 2002* **Lyma Diaeaee National Surveillance Caaa Definition** available at either *NEJM 345 115, 2001* or *JAMA 288 1002 2002*	**If endemic area** if nymphal partially engorged deer tick **doxy** 200 mg po x1 with food	**If not endemic area** not engorged not deer tick No treatment	Prophylaxis study in endemic area erythema migrans developed in 3% of the control group and 0 4% doxy group *(NEJM 345 79 & 133, 2001)*
Early (erythema migrans) *See Comment*		**Doxy** 100 mg bid po or **amoxicillin** 500 mg tid po or **cefuroxime axetil** 500 mg bid or **erythro** 250 mg po qid All regimens for 14–21 d (10 d as good as 20 *AnIM 138 697, 2003)* *See Comment for peds doses*		High rate of clinical failure with azithro & erythro *(Drugs 57 157, 1999)* **Peds** (all for 14–21 d) Amox 50 mg/kg/d in 3 div doses or ceturoxime axetil 30 mg/kg/d in 2 div doses or erythro 30 mg/kg/d in 3 div doses Lesions usually homogenous—not target-like *(AnIM 136 423, 2002)*
Carditis *See Comment*		(**Ceftriaxone** 2 0 gm qd IV) or (**cefotaxime** 2 0 gm q4h IV) or (**pan G** 24 mU qd IV) x14–21 d	**Doxy** *(see Comments)* 100 mg bid x14–21 d or **amoxicillin** 250–500 mg po tid x14–21 d	First degree AV block Oral regimen High degree AV block (PR >0 3 sec) IV therapy—permanent pacemaker not necessary
Facial nerve paralysis (isolated finding early)		(**Doxy** 100 mg bid po) or (**amoxicillin** 500 mg tid po) x14–21 d	**Ceftriaxone** 2 0 gm qd IV x14–21 d	LP suggested to exclude neurologic disease If LP neg oral regimen OK If abnormal or not done suggest parenteral regimen
Meningitis encephalitis *For encephalopathy, see Comment*		**Ceftriaxone** 2 0 gm qd IV x14–28 d	(**Pen G** 20 mU qd in div dose IV) or (**cefotaxime** 2 0 gm q8h IV) x14–28 d	Encephalopathy memory difficulty depression somnolence or headache CSF abnormalities 89% had objective CSF abnormalities 18/18 pts improved with ceftriaxone 2 gm/d x30 d *(JID 180 377 1999)*
Arthritis		(**Doxy** 100 mg bid) or (**amoxicillin** 500 mg qid) po both x30–60 d	(**Ceftriaxone** 2 gm qd IV) or (**pen G** 20–24 mU/d IV) x14–28 d	
Pregnant women	Choice should not include doxy **amoxicillin** 500 mg po tid x21 d			**If pen. allergic:** (**azithro** 500 mg qd x7–10 d) or (**erythro** 500 mg qid po x14–21 d)
Asymptomatic seropositivity and symptoms post-rx		None indicated		No benefit from rx *(NEJM 345 85, 2001)*
Plague **As biological weapon:** *JAMA 283 2281 2000, and Table 1B, page 46*	Yersinia pestis Reservoir rat Vector rat flea	**Gentamicin** 2 0 mg/kg IV loading dose then 1 7 mg/kg q8h IV or **streptomycin** 1 0 gm q12h IM or IV	(**Doxy** 100 mg bid po or IV) or (**chloro** 500 mg qid po or IV)	Reference IV streptomycin *CID 19 1150, 1994* Septicemic form can occur without buboes **CIP** effective in vitro + in animal models *(JAC 41 301 1998)* success in 1 pt *(CID 36 521, 2003)*
Relapsing fever Can be tick borne or louse-borne *(MMWR 52 809, 2003)*	Borrelia recurrentis B hermsii & other borrelia sp	**Doxy** 100 mg bid po	**Erythro** 500 mg qid po	Jarisch-Herxheimer (fever ↑ pulse ↑ resp ↓ blood pressure) in most patients (occurs in ~2 hrs) Not prevented by prior steroids Can relapse up to 10 times **Dx: Examine peripheral blood smear during fever for spirochetes.**

[1] In endemic area (New York) high % of both adult ticks and nymphs were jointly infected with both HGE and B burgdorferi *(NEJM 337 49, 1997)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (39)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (uaual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC FEBRILE SYNDROMES Spread by infected **TICK, FLEA or LICE** *(continued)*				
Rickettsiel diseases				
Spotted tevers (NOTE Rickettsial pox not included)				
Rocky Mountain apotted tevar (RMSF) *(AJTMH 63 21, 2000 ArIM 163 769 2003)*	R rickettsii (Dermacentor ticks)	**Doxy** 100 mg bid po or IV x7 d or for 2 days atter temp normal	**Chloro** use found as risk factor tor tatal RMSF *(JID 184 1437, 2001)*	Fever rash (95%) petechiae 40–50% **Raah apraada from distal extremitiea to trunk.** Dx Immunohisfology on skin biopsy confirmation with antibody titers Highest incidence in Mid-Atlanfic states also seen in Oklahoma S Dakota Montana **NOTE: Only 3–18% ot pts presant with taver, rash, and hx ot tick exposure; esp. in childran many early deatha & ampiric doxy reaeonable** *(MMWR 49 888, 2000)*
NOTE Can mimic ehrlichiosis Pattern of rash important—*see Comment*				
Other spotted fevers e g Boutonneuse fever R africae review *NEJM 344 1504, 2001*	6 species R conorii et al (multiple ticks) In sub-Saharan Africa R africae	**Doxy** 100 mg bid po x7 d	**Chloro** 500 mg qid po/IV x7 d Children <8 y o **azithro** or **clarithro** *(see Comment)*	Clarithro 15 mg/kg/d in 2 div doses & azithro 10 mg/kg/d x1 for 3 days equally efficacious in children with Mediferranean spotted fever *(CID 34 154 2002)* R africae reviews *LnID 3 557, 2003 CID 36 1411 2003* R parkeri in U S *CID 38 805 2004*
Typhua group—Consider in returning travelers with fever				
Louse borne	R prowazekii (body louse)	**Doxy** 100 mg IV/po bid x7 d	**Chloro** 500 mg IV/po qid x7 d	**Brill-Zinsser diaeaae** *(Ln 357 1198 2001)* is a relapse of remote past infection e g WW II Truncal rash spreads centrifugally—opposite of RMSF A winter disease
Murine typhus (cat flea typhus similar)	R typhi (rat reservoir and flea vector)	**Doxy** 100 mg IV/po bid x7 d	**Chloro** 500 mg IV/po qid x7 d	Most U S cases south Texas and southern Calif Flu-like illness Rash in <50% Dx based on suspicion confirmed serologically
Scrub typhus	O tsutsugamushi [rodent reservoir vector is larval stage of mites (chiggers)]	**Doxy** 100 mg IV/po bid x7 d NOTE Reports of doxy and chloro resistance from northern Thailand *(Ln 348 86 1996)* **RIF** alone 450 mg bid po x7 d reported effective *(Ln 356 1057 2000)*		Limited to Far East (Asia India) Cases imported into U S Evidence of chigger bite flu-like illness Rash like louse-borne typhus
Tularamia, typhoidal type Ref **bioterrorism** *see Table 1B page 46 & JAMA 285 2763 2001*	Francisella tularensis (Vector depends on geography ticks biting flies mosquitoes identified)	**Gentamicin** or **tobra** 5 mg/kg/d div q8h IV x7–14 d	Add **chloro** if evidence of meningitis **CIP** reported effective in 12 children *(PIDJ 19 449 2000)*	Typhoidal form in 5–30% pts No lymphadenopathy Diarrhea pneumonia common Dx blood cultures Antibody confirmation Rx Jarisch-Herxheimer reaction may occur Clinical failures with rx with P Ceph 3 *(CID 17 976 1993)*
Urban tranch fever (endocarditis) *(AAC 47 2204 2003)*	Bartonella quintana Vector Body louse	**Gentamicin** 3 mg/kg IV once daily x min of 14 d + **doxy** 200 mg po single daily dose x28 d		One of many Bartonella syndromes *see pages 20 & 38*
Othar Zoonotic Syatemic Bacterial Febrile Illneaaes: Obtain careful epidemiologic history				
Brucellosis *Reviews CID 21 283 1995 EID 3 213 1997)*				
Adult or child >8 years	Brucella sp B abortus—cattle B suis—pigs B melitensis—goats B canis—dogs	[**Doxy** 100 mg bid po x6 wks + **gentamicin** x2–3 wks *(see Table 10C page 72)*] or [**doxy** x6 wks + **streptomycin** 1 0 gm qd IM x2–3 wks] *See Comment*	[**Doxy** + **RIF** 600–900 mg qd po both x6 wks] or [**TMP/SMX** 1 DS tab (160 mg TMP) qid po x6 wks + **gentamicin** x2 wks]	**Relapaaa:** Doxy 100 mg bid po x6 wks + strep 1 0 gm qd IM x2 wks relapse rate 6% With doxy + RIF relapse rate 14% Doxy + RIF may be less effective than doxy + SM in pts with spondylitis *(AnIM 117 25 1992)* CIP alone initially effective but relapse in 25% *(AAC 36 150 1992)* however Oflox + RIF reported effective **Duration ot rx unclear:** For B melitensis gent tor 7 d + doxy for 45 d —fewer relapses than gent x7 d + doxy tor 30 d *(AAC 41 80 1997)* Usual recommendation is 6 wks of rx Longer rx for spondylitis—*see CID 29 1440 1999*
Child <8 years		**TMP/SMX** 5 mg/kg TMP q12h po x6 wks + **gentamicin** 2 mg/kg q8h IV or IM x2 wks		
Leptospiroais *(CID 36 1507 & 1514 2003 LnID 3 757, 2003)*	Leptospira—in urine of domestic livestock dogs small rodents	**Pen G** 1 5 MU IV q6h or **caftriaxona** 1 0 gm qd Duration 7 days	**Doxy** 100 mg q12h IV or po or **AMP** 0 5–1 0 gm q6h IV	**Severity varies** Two-stage mild anicteric illness to severe icteric disease (Weil s disease) with renal failure and myocarditis **Dx:** Culture slow and difficult Sensitivity/specificity ot rapid screening tests poor *(J Clin Micro 40 1464 2002)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (ueual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC FEBRILE SYNDROMES/Other Zoonotic Syatemic Bactarial Febrila Ilinesaes *(continued)*				
Salmonella bactaramia (enteric fever most often caused by S typhi)	Salmonella enteritidis a variety of serotypes	**CIP** 400 mg q12h IV x14 d (switch to po 750 mg bid when clinically possible)	**Ceftriaxone** 2 0 gm qd IV x14 d (switch to po **CIP** when possible)	Usual exposure is contaminated poultry and eggs Many others Myriad of complications to consider e g mycotic aneurysm (10% of adults over age 50 *AJM 110 60 2001*) septic arthritis osteomyelitis septic shock Sporadic reports of resistance to CIP
Miacallaneous Systemic Fabrila Syndromes				
Kawaaaki syndrome 6 weeks to 12 yrs of age peak at 1 yr of age 85% below age 5 *(Ln 364 533 2004)*	Acute self limited vasculitis with ↑ temp rash conjunctivitis stomatitis cervical adenitis red hands/feet & coronary artery aneurysms (25% if untreated)	**IVIG** 2 gm/kg over 12 hrs + **ASA** 80–100 mg/kg/d po div in 4 doses THEN **ASA** 3–5 mg/kg/d po 1x/d x6–8 wks	If still febrile after 1st dose of IVIG some give 2nd dose *(PIDJ 17 1144 1998)*	IV gamma globulin (2 0 gm/kg over 10 hrs) in pts rx before 10th day of illness ↓ coronary artery lesions *(Ln 347 1128 1996)* See *Table 14B page 115* for IVIG adverse effects and expense
Rhaumatic Fevar, acute Ref *CID 33 806 2001*	Post-Group A strep pharyngitis (not Group B C or G)	(1) Symptom relief **ASA** 80-100 mg/kg/d in children 4–8 gm/d in adults (2) Eradicate Group A strep **Pan** x10 d *(see Pharyngitis page 32)* (3) Start prophylaxis *see below*		
Prophylaxis				
Primary prophylaxis	**Benzathina pen G** 1 2 mU IM *(see Pharyngitis p 32)*		**Penicillin** for 10 days prevents rheumatic fever even when started 7–9 days after onset of illness	
Secondary prophylaxis (previous documented rheumatic fever)	**Benzathine pen G** 1 2 mU IM q3–4 wks		Alternative **Penicillin V** 250 mg po bid or **sulfadiazina (sulfisoxazola)** 1 0 gm/d po or **arythro** 250 mg po bid Duration of 2 prophylaxis varies with carditis continue 10 yrs or until age 25 without carditis continue 5 yrs or until age 18 *(AnIM 118 401, 1993)*	
Tumor necrosia factor (TNF) blockada for Crohn s disease rheumatoid arthritis or other	Drugs used Etanercept (Enbrel) infliximab (Remicade) adalimumab (Humira)	Pts at increased risk of reactivation of latent tuberculosis (Tbc) Ideally pts with latent Tbc would delay anti-TNF drugs until Tbc prophylaxis completed *(MMWR 53 683, 2004)*		Suggest TBc history PPD ± chest x-ray prior to initiating TNF blockade Ref *CID 39 295 & 300 2004* Also ↑ risk of histoplasmosis listeria pneumocystis neutropenia pericardial effusion, cutaneous/systemic vasculitis & even myositis from mosquito microsporidium *(NEJM 351 42, 2004)*
Typhoidal ayndroma (typhoid fever enteric fever) *(NEJM 347 1770, 2002)*	Salmonella typhi S para typhi NOTE 14% relapse rate with 5 d ot ceftriaxone *(AAC 44 450, 2000)*	(**CIP** 500 mg bid po x10 d) or (**ceftriaxone** 2 0 gm qd IV x14 d) If associated shock give **daxamethasona** a few minutes before antibiotic *(See Comment)*	**Azithro** 1 gm po day 1 then 500 mg po x6 d *(AAC 43 1441 1999)* or 1 gm po daily x5 d *(AAC 44 1855, 2000)* *(See Comment)*	**Daxamethasone dosa** 3 mg/kg then 1 mg/kg q6h x8 doses ↓ mortality *(NEJM 310 82 1984)* **Complicationa:** perforation of terminal ileum &/or cecum osteo septic arthritis **mycotic aneuryam** (approx 10% over age 50 *AJM 110 62, 2001)* meningitis **Othar rx optiona:** Controlled trial of CIP vs chloro Efficacy equivalent After 5 days blood culture positive CIP 18% chloro 36% *(AAC 47 1727, 2003)* **Children & adolescents: Ceftriaxona** (75 mg/kg/d) and **azithro** (20 mg/kg/d to 1 0 gm max) equal efficacy More relapses with ceftriaxone *(CID 38 951 2004)*
		In children CIP superior to ceftriaxone *(LnID 3 537, 2003)*		
Sepaia: Following suggested **empiric** therapy assumes pt is bacteremic mimicked by viral fungal rickettsial infections and pancreatitis				
Neonatal—early onset <1 week old	Group B strep E coli klebsiella, enterobacter Staph aureus (uncommon) listeria (rare in U S)	**AMP** 25 mg/kg q8h IV + **cetotaxime** 50 mg/kg q12h	(**AMP** + **APAG** 2 5 mg/kg q12h IV or IM) or (**AMP** + **caftriaxona** 50 mg/kg q24h IV or IM)	Blood cultures are key but only 5–10% + Discontinue antibiotics after 72 hrs if cultures and course do not support diagnosis In Spain listeria predominates in S America, salmonella
Neonatal—late onset 1–4 weeks old	As above + H influenzae & S epidermidis	(**AMP** 25 mg/kg q6h IV + **cetotaxime** 50 mg/kg q8h) or (**AMP** + **ceftriaxone** 75 mg/kg q24h IV)	**AMP** + **APAG** 2 5 mg/kg q8h IV or IM	**If MSSA/MRSA a concern, add vanco.**
Child; not neutropenic	Strep pneumoniae meningococci Staph aureus (MSSA & MRSA) H influenzae now rare	(**Catotaxime** 50 mg/kg q8h IV or **ceftriaxone** 100 mg/kg q24h IV) + **vanco** 15 mg/kg IV q6h	**Aztraonam** 7 5 mg/kg IV q6h + **linezolid** *(see Table 16, page 131 for dose)*	Major concerns are S pneumoniae & community-acquired MRSA Coverage for Gm-neg bacilli included but H influenzae infection now rare Meningococcemia mortality remains high *(Ln 356 961, 2000)*

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (41)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usuel)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE[1]	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC FEBRILE SYNDROMES/Sepsis *(continued)*				
Adult; not neutropenic; NO HYPOTENSION—*For Septic Shock, see page 43*				
Source unclear	Aerobic Gm-neg bacilli S aureus streptococci others	(**IMP** or **MER** or **ERTA**) + **vanco**	(**Dapto** IV 6 mg/kg q24h) + (**P Ceph 3/4** or **PIP/TZ** or **TC/CL**)	Systemic inflammatory response syndrome (SIRS) 2 or more of the following 1 Temperature >38°C or <36°C 2 Heart rate >90 beats/min 3 Respiratory rate >20 breaths/min 4 WBC >12,000/μl or >10% bands Sepsis SIRS + a documented infection (+ culture) Severe sepsis Sepsis + organ dysfunction hypotension or hypoperfusion abnormalities (lactic acidosis oliguria ↓ mental status) **Septic shock:** Sepsis induced hypotension (systolic BP <90 mmHg) not responsive to 500 ml IV fluid challenge + peripheral hypoperfusion
		Could sub linezolid for vanco or dapto however linezolid bacteriostatic vs S aureus *Dosages in footnote*[1]		
If suspect biliary source *(see p 10)*	Enterococci + aerobic Gm-neg bacilli	**AM/SB PIP/TZ** or **TC/CL**	**P Ceph 3** + **metro**[1]	
If illicit use IV drugs	S aureus	**Vanco** if high prevalence of MRSA Some empirically use vanco + oxacillin pending susceptibility results		
If suspect intra-abdominal source	Mixture aerobic & anaerobic Gm-neg bacilli	*See secondary peritonitis page 31*		
If petechial rash	Meningococcemia	**Ceftriaxone** 2 0 gm IV q12h (until sure no meningitis), consider Rocky Mountain spotted fever—*see page 40*		
If suspect urinary source	Aerobic Gm-neg bacilli & enterococci	*See pyelonephritis, page 23*		
Neutropenia: Child or adult (absolute PMN count <500/mm³). Guideline: *CID 34:730, 2002*				
Prophylaxis—afebrile				
Post-chemotherapy	Aerobic Gm-neg bacilli pneumocystis (PCP)	Paradox TMP/SMX or FQ works not recommended 2° to ↑ bacterial resistance		TMP/SMX ↓ number of febrile episodes and prevents PCP CIP, Qflox also reported effective but no activity vs PCP Problem is TMP/SMX- & FQ-resistant Gm-neg bacilli
Post-chemotherapy in AIDS patient	↑ risk pneumocystis	**TMP/SMX-DS** po bid—adults 10 mg/kg/d div bid po —children		Need TMP/SMX to prevent PCP Hard to predict which leukemia/lymphoma/solid tumor pt at ↑ risk of PCP
Allogeneic hematopoietic stem cell transplant	↑ risk pneumocystis, herpes viruses candida	**TMP/SMX** as above + (either **acyclovir** or **gancicovir**) + **fluconazole**		Combined regimen justified by combined effect of neutropenia and immunosuppression
Empiric therapy—febrile (≥38.3° C x1 or ≥38° C for ≥1 hr)				
Low-risk adults Peds data pending *(Def low risk in Comment)*	*As above*	**CIP** 750 mg po bid + **AM/CL** 875 mg po bid		**Treat as outpatients with 24/7 access to inpatient care if: no focal findings, no hypotension, no COPD, no fungal infection, no dehydration, age <60 & >16.** Neutropenic children with neg blood cultures safely switched to po cefixime[NUS] 4 mg/kg q12h *(CID 32 36 2001)*
High-risk adults and children	**Aerobic Gm-neg. bacilli; ceph-resistant viridans strep, MRSA**	**Monotherapy: CFP or ceftaz or IMP or MER**	**Combination therapy: (Gent** or **tobra)** + **(TC/CL** or **PIP/TZ)**	Increasing resistance of viridans streptococci to penicillins cephalosporins & FQs *(CID 34 1469 & 1524 2002 CID 31 1126 2000, JAC 47 87 2001)*
		Dosages Footnote[1] and Table 10		**What if severe IgE-mediated β-lactam allergy?** No formal trials but [APAG (or CIP) + aztreonam] ± vanco should work
		Include empiric vanco if suspect IV access infected colonized with DRSP or MRSA blood culture pos for Gm -pos cocci, pt hypotensive		
Persistent fever and neutropenia after 5 days of empiric antibacterial therapy—*see CID 34:730, 2002*				
	Candida species aspergillus	Add either **ampho B** or **voriconazole** *(NEJM 346 225 2002)*		Empirically adding vanco of **no** benefit *(CID 37 382 2003)*

[1] **P Ceph 3** (**cefotaxime** 2 0 gm q8h IV use q4h if life-threatening, **ceftizoxime** 2 0 gm q4h IV **ceftriaxone** 2 0 gm q12h IV) **AP Pen** (**piperacillin** 3 0 gm q4h IV **ticarcillin** 3 0 gm q4h IV) **TC/CL** 3 1 gm q4h IV **PIP/TZ** 3 375 gm q4h IV **AM/SB** 3 0 gm q6h IV **APAG** *(see Table 10C page 72)* **AMP** 30 mg/kg q4h IV **clinda** 900 mg q8h IV **IMP** 0 5 gm q6h IV **MER** 1 0 gm q8h IV **Natcillin** or **oxacillin** 2 0 gm q4h IV **aztreonam** 2 0 gm q8h IV **metro** 1 0 gm loading dose then 0 5 gm q6h or 1 0 gm q12h IV **vanco** 1 0 gm q12h IV **P Ceph 3 AP** (**ceftazidime** 2 0 gm q8h IV) **P Ceph 4** [**CFP** 2 0 gm q12h (q8h if neutropenic) IV **cefpirome**[NUS] 2 0 gm q12h IV] **CIP** 400 mg q12h IV **oflox** 400 mg q12h IV **levo** 750 mg qd **linezolid** 600 mg q12h IV

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 1 (42)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (usual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC FEBRILE SYNDROMES *(continued)*				
Shock syndromes				
Septic shock: Fever & hypotension Bacteremic shock endotoxin shock Revs *Ln 351 1501 1998 NEJM 340 207, 1999* Activ Protein C *Med Lett 44 17 2002*	Bacteremia with aerobic Gm neg bacteria or Gm+ cocci	**Proven therapy: (1) Replete intravascular volume, (2) correct, if possible, disease that allowed bloodstream invasion, (3) appropriate empiric antimicrobial rx** *see suggestions under life-threatening sepsis, above* **(4)** For recombinant **activated Protein C** (drotrecogin alfa) see *Comment* **(5) Investigational: low-dose steroids** if document relative adrenal insufficiency *(see Comment for criteria)* [Hydrocortisone 50 mg IV q6h + fludrocortisone (Florinef) 50 µg via NG once daily] x7 d (6) Low-dose **vasopressin** reported effective for catecholamine-resistant septic shock *(Ln 359 1209 2002)*		**Activ. Protein C: Drotrecogin (Xigris):** In a prospective randomized double blind study *(NEJM 344 699, 2001)* 28 d mortality ↓ from 31 to 25% in sickest pts Study in less ill pts showed no benefit Speculation benefit in pts with low or decreasing levels of activ protein C (protein C levels not routinely available) **Hemorrhage** (3.5% drotrecogin 2% placebo) **Dose** 24 µg/kg/hr over 96 hrs by continuous IV infusion Stop 2 hrs before & restart 12 hrs after surgery Approx **cost** of drug for 4-day course $8000 **Low-dose steroids** In controlled random double-blind trial rx if low baseline cortisol & ≤9 µg/dl response to 250 mg IV cosyntropin 28-day mortality 63% placebo & 53% steroid group *(JAMA 288 862 & 886 2002)* Results in question because total & not "free" plasma cortisol was measured *(NEJM 350 1601 & 1629 2004)* **Low-dose vasopressin:** Dose should not exceed 0.04 units/min
Septic shock: post-splenectomy (asplenia)	S pneumoniae N meningitidis H influenzae Capnocytophaga (DF-2)	**Ceftriaxone** 2 0 gm IV qd (↑ to 2 0 gm q12h if meningitis)	(**Gati** 400 mg or **Levo** 750 mg or **Moxi** 400 mg) all once daily IV	Howell-Jolly bodies in peripheral blood smear confirm absence of functional spleen Often results in **aymmetrical peripheral gangrene of digits** due to severe DIC For prophylaxis, *see Table 15A, page 123*
Toxic shock syndrome, staphylococcal. Superantigen review *LnID 2 156 2002* Colonization by toxin producing Staph aureus of vagina (tampon-assoc) surgical/traumatic wounds endometrium burns	Staph aureus (toxic shock toxin-mediated)	(**Nafcillin** or **oxacillin** 2 0 gm q4h IV) or (if MRSA **vanco** 1 0 gm IV q12h) + **IVIG**	(**Cefazolin** 1–2 gm q8h IV) or (if MRSA **vanco** 1 0 gm IV q12h) + **IVIG**	Natcillin/oxacillin/cefazolin have no effect on initial syndrome but ↓ recurrences Seek occult abscess TSS may occur with "clean" colonized post-op wounds Case fatality 5–15% **IVIG reasonable** *(see Streptococcal TSS)*— dose 1 0 gm/kg day 1, then 0 5 gm/kg days 2 & 3
Toxic shock syndrome, streptococcal [Ref *JID 179(Suppl 2) S366–374, 1999*] NOTE For necrotizing fasciitis without toxic shock see *page 38* Associated with invasive disease i e erysipelas necrotizing fasciitis, secondary strep infection of varicella Secondary cases TSS reported *(NEJM 335 547 & 590, 1996 CID 27 150 1998)*	Group A B C & G Strep pyogenes	(**Pen G** 24 mU/d IV in div doses) + (**clinda** 900 mg q8h IV) **IVIG** associated with ↓ in sepsis-related organ failure *(CID 37 333 & 341 2003)* IVIG dose 1 gm/kg day 1 then 0 5 gm/kg days 2 & 3	**Ceftriaxone** 2 0 gm q24h IV + **clinda** 900 mg q8h IV	Definition Isolation of Group A strep hypotension and ≥2 of renal impairment coagulopathy liver involvement ARDS generalized rash soft tissue necrosis *(JAMA 269 390, 1993)* Associated with invasive disease **Surgery usually required.** Mortality with fasciitis 30–50% myositis 80% even with early rx *(CID 14 2 1992)* Clinda ↓ toxin production Use of NSAID may predispose to TSS For discussion of possible reasons pen G may fail in fulminant S pyogenes infections, see *JID 167 1401, 1993)*
Other Toxin-Mediated Syndromes—no fever unless complicated				
Botulism *(AnIM 129 221 1998 CID 31 1018 2000 As **biologic weapon** JAMA 285 1059, 2001, Table 1B, page 46 www bt cdc gov)*				
Food-borne Dyspnea at presentation bad sign *(CID 39 357 & 363 2004)* **Infant**	C botulinum	For all types Follow vital capacity other supportive care If no ileus purge GI tract Human botulinum immunoglobulin (BIG) IV, single dose Call 510 540 2646 Do not use equine antitoxin	Trivalent (types A B E) equine serum antitoxin— State Health Dept or CDC *(see Comment)* No antibiotics may lyse C botulinum in gut and ↑ load of toxin	**Equine antitoxin:** Obtain from State Health Depts or CDC (404-639 2206 M-F OR 404-639-2888 evenings/weekends) Skin test first & desensitize if necessary One vial IV and one vial IM **Antimicrobials:** May make infant botulism worse Untested in wound botulism When used pen G 10–20 MU/d usual dose If complications (pneumonia UTI) occur avoid antimicrobials with assoc neuromuscular blockade i e aminoglycosides tetracycline **Differential dx:** Guillain-Barre, myasthenia gravis tick paralysis organophosphate toxicity West Nile virus

(Footnotes and abbreviations on page 45)

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 1 (43)

ANATOMIC SITE/DIAGNOSIS/ MODIFYING CIRCUMSTANCES	ETIOLOGIES (ueual)	SUGGESTED REGIMENS* PRIMARY	SUGGESTED REGIMENS* ALTERNATIVE†	ADJUNCT DIAGNOSTIC OR THERAPEUTIC MEASURES AND COMMENTS
SYSTEMIC FEBRILE SYNDROMES/Othar Toxin-Madiated Syndromes/Botulism *(continued)*				
Wound		Debridement & anaerobic cultures No proven value of local antitoxin Role of antibiotics untested	Trivalent equine antitoxin *(see Comment)*	Can result from spore contamination of tar heroin
Tatanus	C tetani	**Pen G** 24 mU in div dose or **doxy** 100 mg q12h IV x7–10 d	**Metro** 500 mg q6h po or 1 0 gm q12h IV x7–10 d *(See Comment)*	Multifaceted treatment Wound debridement tetanus immunoglobulin (250–500 IU IM) antimicrobics & tetanus toxoid (tetanus does not confer immunity) Options for control of muscle spasms continuous infusion of midazolam IV propotol and/or intrathecal baclofen *(CID 38 321, 2004)*
VASCULAR				
Cavernous sinus thrombosis	Staph aureus Group A strep H influenzae asper gillus/mucor/rhizopus	**Vanco** 1 0 gm IV q12h + **ceftriaxone** 2 0 gm IV qd	**(Dapto** 6 mg/kg IV qd[NAI] or **linezolid** 600 mg IV q12h) + **ceftriaxone** 2 0 gm IV qd	CT or MRI scan for diagnosis Heparin indicated *(Ln 338 597 1991)* If patient diabetic with ketoacidosis or post-desferrioxamine rx or neutropenic consider fungal etiology, as aspergillus mucor rhizopus, *see Table 11A pages 73 & 80*
IV line infection *(see IDSA Guidelines CID 32 1249 2001)*: **Treatment**				
Heparin lock midline catheter non tunneled central venous catheter (subclavian internal jugular) peripherally inserted central catheter (PICC) Avoid temoral vein if possible ↑ risk of infection and/or thrombosis *(JAMA 286 700 2001)*	Staph epidermidis Staph aureus (MSSA/MRSA)	**Vanco** 1 0 gm q12h IV **Linezolid alternative—see Comment.** Other rx and duration **(1) If S. aureus** remove catheter Can use TEE result to determine if 2 or 4 wks of rx **(2) If S. epidermidis** can try to "save" catheter 80% cure after 7–10 d of rx Catheter-hub/lumen Infections may respond to "antibiotic lock" rx & allow salvage of catheter *(JAC 48 597 2001)* Drug (**vanco gent CIP**) at 1–5 mg/ml mixed with 50–100 units heparin (or saline) in 2–5 ml volume fill catheter when not in use Continue 2 wks **For S. aureua, need full coursa of parenteral therapy** If candida *see Hyperalimentation below and Table 11A pages 74–75*	**Linezolid has predictable bacteriostatic activity va most S. aureus and S. epidermidis isolates—including MRSA/MRSE. Authors prefer vanco in order to ↑ longevity of linezolid activity. If MRSA/MRSE and either failure of vanco rx or vanco allergy, linezolid dose 600 mg IV/po q12h.** Culture removed catheter With roll method >15 colonies *(NEJM 312 1142 1985)* suggests infection Lines do not require "routine" changing when not infected When infected do not insert new catheter over a wire Antimicrobial impregnated catheters may ↓ infection risk the debate is lively *(CID 37 65, 2003 & 38 1287, 2004)*
Tunnel type indwelling venous catheters and ports (Broviac Hickman Groshong Quinton) dual lumen hemodialysis catheters (Perma-cath)	Staph epidermidis Staph aureus (Candida sp) Rarely leuconostoc or lacto bacillus—both resistant to vanco *(see Table 2)*			**If S. epidermidis & catheter left in, vanco can cure 80%** of infections limited to exit site but only 25% cure if infection in subcutaneous tunnel between skin and subclavian vein **If S. aureus & catheter left in, vanco cure rata 10% at exit aite & 0% with tunnel infection** *(AJM 89 137, 1990)* Similar statistics for infected ports *(CID 29 102 1999)* Infected hemodialysis access catheters should be removed *(AnIM 127 275 1997)*
Impaired host (burn neutropenic)	As above + Pseudomonas sp Enterobacteriaceae Corynebacterium jeikeium aspergillus rhizopus	(**Vanco** + **P Ceph 3 AP**) or (**vanco** + **AP Pen**) or **IMP** or (**P Ceph 3** + **APAG**) *(Dosage see page 42)*		Usually have associated septic thrombophlebitis Biopsy of vein to rule out fungi If fungal surgical excision + amphotericin B Surgical drainage ligation or removal often indicated
Hyperalimentation	As with tunnel + Candida sp common *(see Table 11 resistant Candida species)*	If candida **amphotericin B** 0 5–0 6 mg/kg qd IV total dose 5 0 mg/kg or **voriconazole** 3 mg/kg bid IV or **caspotungin** 70 mg IV day 1 then 50 mg IV qd		Remove venous catheter and discontinue antimicrobial agents if possible Ophthalmologic consultation recommended **Rx all patiants with + blood cultures.** *See Table 11A Candidiasis*
Intravenous lipid emulsion	Staph epidermidis Malassezia furfur	**Vanco** 1 0 gm q12h IV **Amphotericin B**		Discontinue intralipid *AJM 90 129, 1991*
IV line infection: Prevention *(CID 35 1281 2002 NEJM 348 1123 2003)* To minimize risk of infection	1 Maximal sterile barrier precautions during catheter insertion 2 Use 2% chlorhexidine for skin antisepsis 3 If infection rate high despite #1 & 2 use either chlorhexidine/silver sulfadiazine or minocycline/rifampin impregnated catheters			Tunneled hemodialysis catheters Small study ↓ infection rate when catheter locked with gentamicin (5 mg/ml) + heparin 5000 IU/ml) p < 0 02 *(Kidney Intl 66 801 2004)*
Septic pelvic vein thrombophlebitis (with or without septic pulmonary emboli) Postpartum or postabortion or postpelvic surgery	Streptococci bacteroides Enterobacteriaceae	**Metro** + **P Ceph 3 cefoxitin TC/CL PIP/TZ** or **AM/SB**	**IMP** or **MER** or **ERTA** or [(**clinda** + (**aztreonam** or **APAG**)]	Use heparin during antibiotic regimen Continued oral anticoagulation not recommended Cefotetan less active than cefoxitin vs non fragilis bacteroides Cefotetan and cefmetazole have methyltetrazole side chain which is associated with hypoprothrombinemia (prevent with vitamin K)

(Footnotes and abbreviations on page 45) *NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function* **NAI** = *Not FDA-approved indication*

TABLE 1 (44): FOOTNOTES AND ABBREVIATIONS

* **Dosages suggested are for adults** (unless otherwise indicated) with clinically severe (often life threatening) infections. Dosages also assume normal renal function and not severe hepatic dysfunction. *See Table 16, page 131* for pediatric dosages. **Dosage abbreviations: qd** = once daily; **bid** = twice a day; **tid** = three times a day; **qid** = four times a day

§ **Alternative therapy** includes these considerations: allergy, pharmacology/pharmacokinetics, compliance, costs, local resistance profiles

AHA = American Heart Association
AM/CL = amox/clav (Augmentin) ***AM/CL-ER*** (Augmentin XR)
AM/SB = ampicillin/sulbactam (Unasyn)
Amox = amoxicillin
AMP = ampicillin
APAG = antipseudomonal aminoglycosidic antibiotics
AP Pen = antipseudomonal β-lactamase susceptible penicillins, e.g., piperacillin *See Table 4, page 52 for details*
ARDS = adult respiratory distress syndrome
ARF = acute rheumatic fever
ASA = acetylsalicylic acid (aspirin)
ASD = antistreptolysin O
Azithro = azithromycin
Ceftaz = ceftazidime
CFP = cefepime
Chloro = chloramphenicol
CIP = ciprofloxacin ***CIP-ER*** = ciprofloxacin extended release
Clarithro = clarithromycin ***clarithro ER*** = clarithromycin extended release
Clinda = clindamycin
C&S = culture and sensitivities
CSD = cat-scratch disease *(see page 30)*
Dapto = daptomycin
DIC = disseminated intravascular coagulation
Doxy = doxycycline
DRSP = drug resistant Streptococcus pneumoniae
DS = double-strength
EBV = Epstein-Barr virus
EDC = expected date of confinement
EES = erythromycin ethyl succinate
ERTA = ertapenem
Erythro = erythromycin
ETB = ethambutol
FQ = fluoroquinolone
GAS = Group A streptococci
Geti = gatifloxacin
GC = gonorrhea (N. gonorrhoeae)
Gemi = gemifloxacin
GNB = Gram-negative bacilli
HHV-2 = human herpesvirus 2
HIV-1 = human immunodeficiency virus type 1
HLR = high-level resistance
I = investigational
IMP = imipenem cilastatin (Primaxin)
INH = isoniazid
IVDU = intravenous drug users
IVIG = intravenous immune globulin
LCM = lymphocytic choromeningitis virus
LCR = ligase chain reaction
Levo = levofloxacin
Macrolides = erythro, azithro, clarithro, dirithro
MER = meropenem
Metro = metronidazole
Moxi = moxifloxacin
MRI = magnetic resonance imaging
MSSA/MRSA = methicillin-sensitive/methicillin-resistant Staph aureus
MSSE/MRSE = methicillin-sensitive/methicillin-resistant Staph epidermidis
MTBc = Mycobacterium tuberculosis
NAI = Not FDA approved indication
NF = nitrofurantoin
NSAIDs = nonsteroidal anti-inflammatory drugs
NUS = not available in the United States
O Ceph 1, 2, 3 = oral cephalosporins—*see Table 9B, page*
Oflox = Ofloxacin
P Ceph 1, 2, 3 = parenteral cephalosporins—*see Table 9B, pages 64, 65*
P Ceph 3 AP = third generation with enhanced antipseudomonal activity
P Ceph 4 = third generation with antistaphylococcal and antipseudomonal activity
PCR = polymerase chain reaction
PIP/TZ = piperacillin/tazobactam
Q/D = quinupristin/dalfopristin
Rick = rickettsia (spotted fever, Q fever)
RIF = rifampin
R/O = rule out
SA = Staph. aureus
SM = streptomycin
STD = sexually transmitted diseases
TBc = tuberculosis
TC/CL = ticarcillin/clavulanate (Timentin)
TEE = transesophageal echocardiography
Telithro = telithromycin
TMP/SMX = trimethoprim/sulfamethoxazole
Tobra = tobramycin
Toxo = toxoplasmosis
UTI = urinary tract infection
Venco = vancomycin

ABBREVIATIONS OF JOURNAL AND TEXT TITLES

AAC Antimicrobial Agents & Chemotherapy
Adv PID Advances in Pediatric Infectious Diseases
AIDS AIDS
AJM American Journal of Medicine
AJRCCM American Journal of Respiratory Critical Care Medicine
AJTMH American Journal of Tropical Medicine & Hygiene
AnEM Annals of Emergency Medicine
AnIM Annals of Internal Medicine
AnSurg Annals of Surgery
ArIM Archives of Internal Medicine
ARRD American Review of Respiratory Disease
CCM Critical Care Medicine
CID Clinical Infectious Diseases
COID Current Opinion in Infectious Disease
CTID Clinical Topics in Infectious Disease
DMID Diagnostic Microbiology and Infectious Disease
EID Emerging Infectious Diseases
EJCMID European Journal of Clin. Micro. & Infectious Diseases
Gestro Gastroenterology
ICHE Infection Control and Hospital Epidemiology
IDC No. Amer Infectious Disease Clinics of North America
IDCP Infectious Diseases in Clinical Practice
J Clin Micro Journal of Clinical Microbiology
J Ped Journal of Pediatrics
JAC Journal of Antimicrobial Chemotherapy
JAMA Journal of the American Medical Association
JAVMA Journal of the Veterinary Medicine Association
JID Journal of Infectious Diseases
JNS Journal of Neurosurgery
JTMH Journal of Tropical Medicine and Hygiene
Ln Lancet
LnID Lancet Infectious Disease
Med Lett Medical Letter
MMWR Morbidity & Mortality Weekly Report
NEJM New England Journal of Medicine
Peds Pediatrics
PIDJ Pediatric Infectious Disease Journal
QJM Quarterly Journal of Medicine
SMJ Southern Medical Journal
TRSM Transactions of the Royal Society of Medicine

TABLE 1B: PROPHYLAXIS AND TREATMENT OF ORGANISMS OF POTENTIAL USE AS BIOLOGICAL WEAPONS

DISEASE	ETIOLOGY	SUGGESTED EMPIRIC TREATMENT REGIMENS		SPECIFIC THERAPY AND COMMENTS
		PRIMARY	ALTERNATIVE	
Anthrax **Cutaneous, inhalational, gastrointestinal** Refs *JAMA 286 2549, 2554 & 2595, 2001, MMWR 50 909 2001, NEJM 345 1607 & 1621, 2001 CID 35 851, 2002* or www bt cdc gov Also see *Table 1, pages 28 & 34* To report bioterrorism event 770 488-7100 Rationale for CIP *CID 39 303, 2004*	Bacillus anthracis Post-exposure **prophylaxis** Ref *Med Lett 43 91, 2001*	**Adults (including pregnancy): CIP** 500 mg po bid x60 d **Children: CIP** 20–30 mg/kg/d div q12h x60 d	**Adults (including pregnancy): Doxy** 100 mg po bid x60 d **Children** *(see Comment)* **Doxy** >8 y/o & >45 kg 100 mg po bid >8 y/o & ≤45 kg 2 2 mg/kg po bid ≤8 y/o 2 2 mg/kg po bid All for 60 days	1 Once organism shows susceptibility to penicillin, switch children to **amoxicillin** 80 mg/kg/d div q8h (max 500 mg q8h) switch pregnant pt to **amoxicillin** 500 mg po tid 2 Do **not** use cephalosporins or TMP/SMX 3 Other **FQs** (Gati Levo Moxi)) & clarithro should work but no clinical experience
	Treatment— **Cutaneous** anthrax *NEJM 345 1611 2001*	**Adults (including pregnancy): CIP** 500 mg po bid x60 d **Children CIP** 20–30 mg/kg/d div q12h po (to max 1 gm/d) x60 d	**Adults (including pregnancy): Ooxy** 100 mg po bid x60 d **Children Ooxy** >8 y/o & >45 kg 100 mg po bid, >8 y/o & ≤45 kg 2 2 mg/kg po bid ≤8 y/o 2 2 mg/kg po bid All for 60 days	1 If penicillin susceptible then **Adults: Amox** 500 mg po q8h x60 d **Children: Amox** 80 mg/kg/d div q8h (max 500 mg q8h) 2 Usual treatment of cutaneous anthrax is 7–10 d , 60 d in setting of bioterrorism with presumed aerosol exposure 3 Other **FQs** (Gati Levo, Moxi) should work based on in vitro susceptibility data
	Treatment—**Inhalational** gastrointestinal or oropharyngeal Characteristic signs & symptoms—**Preaent** Dyspnea N/V **Abaent** Rhinorrhea sore throat *(AnIM 139 337, 2003)*	**Adults (including pregnancy):** (**CIP** 400 mg IV q12h) or (**doxy** 100 mg IV q12h) + **clinda** 900 mg IV q8h + **RIF** 300 mg IV q12h Switch to po when able & ↓ **CIP** to 500 mg po bid **clinda** to 450 mg po q8h & **RIF** 300 mg po bid Treat x60 days *See Table 2 page 47 for other alternatives*	**Children** (**CIP** 10 mg/kg IV q12h or 15 mg/kg po q12h) or (**Ooxy** >8 y/o & >45 kg 100 mg IV q12h >8 y/o & ≤45 kg 2 2 mg/kg IV q12h ≤8 y/o 2 2 mg/kg IV q12h) **plus clindamycin** 7 5 mg/kg IV q6h **plus RIF** 20 mg/kg (max 600 mg) IV qd Treat x60 d *See Table 16 page 131 for oral dosage*	1 Clinda may block toxin production 2 Rifampin penetrates CSF & intracellular sites 3 If isolate shown penicillin-susceptible a **Adult: Pen G** 4 mU IV q4h b **Child: Pan G** <12 y/o 50 000 U/kg IV q6h >12 y/o 4 mU IV q4h c Constitutive & inducible β lactamases--do not use pen or AMP alone 4 Do not use cephalosporins or TMP/SMX 5 Erythro, azithro activity borderline clarithro active 6 No person-to-person spread
Botulism Ref *JAMA 285 1059 2001* Food borne[1] *See Table 1, pages 43–44*	Clostridium botulinum	Purge GI tract if no ileus **Trivalent antitoxin** (types A B, & E) single 10 ml vial/pt diluted in saline IV (slowly)	Antibiotics have no effect on toxin	Supportive care for all types Follow vital capacity Submit suspect food for toxin testing Ref *CID 39 357 & 363 2004*
Hemorrhagic fever viruses Ref *JAMA 287 2391, 2002*	Ebola, Lassa, Hanta yellow fever & others	Fluid/electrolyte balance Optimize circulatory volume	For Lassa & Hanta **Ribavirin** dose same as Adults Pregnancy Children LD 30 mg/kg (max 2 gm) IV x1, then 16 mg/kg IV (max 1 gm/dose) q6h x4 d then 8 mg/kg IV (max 500 mg) q8h x6 d	Ribavirin active in vitro, not FDA approved for this indication NOTE Ribavirin contraindicated in pregnancy However in this setting the benefits outweigh the risks
Plague Ref *JAMA 283 2281 2000* Inhalation pneumonic plague[1] *See Table 1, page 39*	Yersinia pestis **Treatment**	**Gentamicin** 5 mg/kg IV qd or **streptomycin** 15 mg/kg IV bid Tobramycin should work	(**Doxy** 200 mg IV x1 & then 100 mg po or IV bid) or (**CIP** 500 mg po bid or 400 mg IV q12h)	1 **Chloro** also active 25 mg/kg IV qid 2 In mass casualty situation may have to treat po 3 Pediatric doses *see Table 16 page 131* 4 Pregnancy *as for non-pregnant adults* 5 Isolate during first 48 hrs of treatment
	Post-exposure prophylaxis	**Doxy** 100 mg po bid x7 d	**CIP** 500 mg po bid x7 d	For community with pneumonic plague epidemic Pediatric doses *see Table 16 page 131* Pregnancy *As for non pregnant adults*
Smallpox Ref *NEJM 346 1300 2002* *See Comment*	Variola virus	Smallpox vaccine up to 4 days after exposure Isolation, gloves gown & NAS respirator	**Cidofovir** protected mice against aerosol cowpox *(JID 181 10 2000)*	***Immediately notify State Health Dept.*** & State notifies CDC (770-488 7100) Vaccinia immune globulin of no benefit For vaccination complications, see *JAMA 288 1901, 2002*
Tularemia Inhalational tularemia[1] Ref *JAMA 285 2763 2001* *See Table 1 page 40*	Francisella tularemia **Treatment**	(**Streptomycin** 15 mg/kg IV bid) or (**gentamicin** 5 mg/kg IV qd) x10 d	**Doxy** 100 mg IV or po bid x14–21 d or **CIP** 400 mg IV (or 750 mg po) bid x14–21 d	For pediatric doses *see Table 16 page 131* Pregnancy *As for non-pregnant adults* **Tobramycin** should work
	Post-exposure prophylaxis	**Doxy** 100 mg po bid x14 d	**CIP** 500 mg po bid x14 d	For pediatric doses, *see Table 16 page 131* Pregnancy *As for non-pregnant adults*

[1] There are other clinical forms of botulism plague, and tularemia but the inhalation form seems most probable in bioterrorism

TABLE 2. RECOMMENDED ANTIMICROBIAL AGENTS AGAINST SELECTED BACTERIA

BACTERIAL SPECIES	ANTIMICROBIAL AGENT *(See footnote[2] for abbreviations)*		
	RECOMMENDED	ALTERNATIVE	ALSO EFFECTIVE[1] (COMMENTS)
Alcaligenes xylosoxidans (Achromobacter xylosoxidans)	IMP MER AP Pen	TMP/SMX Some strains susc to ceftaz *(AAC 32 276, 1988)*	Resistant to APAG P Ceph 1 2 3 4 aztreonam FQ *(AAC 40 772, 1996)*
Acinetobacter calcoaceticus–baumannii complex	IMP or MER or [FQ + (amikacin or ceftaz)]	AM/SB *(CID 24 932 1997)* Sulbactam[NUS] also effective *(JAC 42 793 1998)* colistin *(CID 36 1111, 2003)*	Polymyxin B up to 5% isolates resistant to IMP resistance to FQs, amikacin increasing Doxy + amikacin effective in animal model *(JAC 45 493 2000)* *(See Table 5, page 55)*
Actinomyces israelii	AMP or Pen G	Doxy, ceftriaxone	Clindamycin, erythro
Aeromonas hydrophila	FQ	TMP/SMX or (P Ceph 3 4)	APAG, ERTA IMP MER tetracycline (some resistant to carbapenems)
Arcanobacterium (C.) haemolyticum	Erythro	Benzathine Pen G	Sensitive to most drugs resistant to TMP/SMX *(AAC 38 142, 1994)*
Bacillus anthracis (anthrax) inhalation	*See Table 1B page 46*		
Bacillus cereus B. subtilis	Vancomycin clindamycin	FQ IMP	
Bacteroides fragilis (ssp fragilis)	Metronidazole	Clindamycin	Cefoxitin, ERTA IMP MER TC/CL PIP/TZ AM/SB cefotetan AM/CL
DOT[1] group of bacteroides[2]			(not cefotetan)
Bartonella (Rochalimaea) henselae, quintana *See Table 1 pages 30, 34 38*	Azithro or clarithro or CIP (bacillary angiomatosis) or azithro (cat-scratch) *(PIDJ 17 447 1998 AAC 48 1921, 2004)*	Erythro or doxy	Other drugs TMP/SMX *(IDC No Amer 12 137, 1998)* Consider doxy + RIF for severe bacillary angiomatosis *(IDC No Amer 12 137 1998)* doxy + gentamicin optimal for endocarditis *(AAC 47 2204, 2003)*
Bordetella pertussis	Erythro	TMP/SMX	An erythro-resistant strain reported in Arizona *(MMWR 43 807, 1994)*
Borrelia burgdorferi, B. afzelii, B. garinii	Ceftriaxone cefuroxime axetil doxy amox *(See Comments)*	Penicillin G (HD) cefotaxime	Clarithro Choice depends on stage of disease *Table 1, page 39*
Borrelia sp	Doxy	Erythro	Penicillin G
Brucella sp	Doxy + either gentamicin or streptomycin *(IDCP 7 2004)*	(Doxy + RIF) or (TMP/SMX + gentamicin)	FQ + RIF *(AAC 41 80 1997, Emerg ID 3 213 1997 CID 21 283 1995)* Minocycline + RIF *(J Chemother 15 248, 2003)*
Burkholderia (Pseudomonas) cepacia	TMP/SMX or MER or CIP	Minocycline or chloramphenicol	(Usually resistant to APAG AG polymyxins) *(AAC 37 123 1993 & 43 213, 1999 Inf in Med 18 49 2001)* (Some resistant to carbapenems) Combination rx may be necessary *(AJRCCM 161 1206, 2000)*
Burkholderia (Pseudomonas) pseudomallei *See Table 1 page 27 & Ln 361 1715 2003*	Initially IV ceftaz or IMP *(CID 29 381 1999)*	Then, combination of po chloro doxy & TMP/SMX	(In Thailand 12–80% strains resistant to TMP/SMX) FQ active in vitro Combination of chloro TMP/SMX, doxy more effective than doxy alone for maintenance rx *(CID 29 375, 1999)* MER also effective *(AAC 48 1763,2004)*
Campylobacter jejuni	Erythro	FQ (↑ resistance *NEJM 340 1525,1999*)	Clindamycin, doxy, azithro, clarithro *(see Table 5 page 55)*
Campylobacter fetus	IMP	Gentamicin	AMP chloramphenicol erythro
Capnocytophaga ochracea (DF-1) and	Clindamycin or AM/CL	CIP Pen G	P Ceph 3 IMP cefoxitin, FQ, (resistant to APAG TMP/SMX) C. hemolytica & C. granulosa are often resistant to β-lactams & aminoglycosides [*CID 35(Suppl 1) S17, 2002*]
canimorsus (DF-2)	AM/CL		
Chlamydophila pneumoniae	Doxy	Erythro FQ	Azithro clarithro, telithro
Chlamydia trachomatis	Doxy or azithro	Erythro or oflox	Levofloxacin
Chryseobacterium (Flavobacterium) meningosepticum	Vancomycin ± RIF *(CID 26 1169 1998)*	CIP, levofloxacin	In vitro susceptibilities may not correlate with clinical efficacy *(AAC 41 1301, 1997, CID 26 1169, 1998)*
Citrobacter diversus (koseri) C. freundii	CARB	FQ	APAG
Clostridium difficile	Metronidazole (po)	Vancomycin (po)	Bacitracin (po)
Clostridium perfringens	Pen G ± clindamycin	Doxy	Erythro chloramphenicol cefazolin, cefoxitin, AP Pen CARB
Clostridium tetani	Metronidazole or Pen G	Doxy	CARB
Corynebacterium jeikeium	Vancomycin	Pen G + APAG	
C. diphtheriae	Erythro	Clindamycin	RIF Penicillin reported effective *(CID 27 845, 1998)*
Coxiella burnetii (Q fever) acute disease	Doxy *(see Table 1 page 20)*	Erythro	In meningitis consider FQ *(CID 20 489 1995)* Endocarditis doxy + hydroxychloroquine *(JID 188 1322 2003, LnID 3 709 2003)*
chronic disease	(CIP or doxy) + RIF	FQ + doxy x3 yrs *(CID 20 489 1995)*]	Chloroquine + doxy *(AAC 37 1773 1993)* ? gamma interferon *(Ln 20 546, 2001)*

TABLE 2 (2)

BACTERIAL SPECIES	ANTIMICROBIAL AGENT *(See footnote[2] for abbreviations)*		
	RECOMMENDED	**ALTERNATIVE**	**ALSO EFFECTIVE[1] (COMMENTS)**
Ehrlichia chaffeensis Ehrlichia ewubguum Anaplasma (Ehrlichia) phagocytophilum	Doxy	Tetracycline RIF *(CID 27 213 1998)*	CIP oflox chloramphenicol also active in vitro Resistant to clinda TMP/SMX IMP AMP erythro & azithro *(AAC 41 76 1997)*
Eikenella corrodens	Penicillin G or AMP or AM/CL	TMP/SMX FQ	Doxy cefoxitin cefotaxime IMP (Resistant to clindamycin cephalexin erythromycin and metronidazole)
Enterococcus faecalis	*See Table 5 page 54*		
Enterococcus faecium β-lactamase + high-level aminoglycoside resist vancomycin resist *See Table 5, page 54*			
Erysipelothrix rhusiopathiae	Penicillin G or AMP	P Ceph 3 FQ	IMP AP Pen (vancomycin APAG TMP/SMX resistant)
Francisella tularensis (tularemia) *See Table 1B page 46*	Gentamicin tobramycin or streptomycin	Doxy or CIP	Chloramphenicol RIF Doxy/chloro bacteriostatic → relapses
Gardnerella vaginalis (bacterial vaginosis)	Metronidazole	Clindamycin	*See Table 1 page 17 for dosage*
Hafnia alvei	*Same as Enterobacter spp*		
Helicobacter pylori	*See Table 1, page 13*		Drugs effective in vitro often fail in vivo
Hemophilus aphrophilus	[(Penicillin or AMP) ± gentamicin] or [AM/SB ± gentamicin]	P Ceph 2 3 ± genfamicin	(Resistant to vancomycin clindamycin methicillin)
Hemophilus ducreyi (chancroid)	Azithro or ceftriaxone	Erythro CIP	Most strains resistant to tetracycline amox TMP/SMX
Hemophilus influenzae Meningitis epiglottitis & other life-threatening illness	Cefotaxime ceftriaxone	TMP/SMX CARB FQs (AMP if β-lactamase negative) (U S 25–30% AMP resistance Japan 35%)	Chloramphenicol (downgraded from 1st choice because of hematotoxicity) 9% of U S strains resistant to TMP/SMX *(AAC 41 292 1997)*
non-life threatening illness	AM/CL Q Ceph 2/3 TMP/SMX AM/SB		Azithro clarithro telithro
Klebsiella ozaenae/rhino scleromatis	FQ	RIF + TMP/SMX	*(Lancet 342 122 1993)*
Lactobacillus sp	(Pen G or AMP) ± gentamicin	Clindamycin erythro	**May be resistant to vancomycin**
Legionella sp. *(42 species & 60 serotypes recognized) (Sem Resp Inf 13 90, 1998)*	FQ or azithro or (erythro ± RIF)	Clarithro telithro	TMP/SMX doxy Most active FQs in vitro Gemi Gati Levo Moxi *See AnIM 129 328, 1998*
Leptospira interrogans	Penicillin G	Doxy	Ceftriaxone *(CID 36 1507 2003)*
Leuconostoc	Pen G or AMP	Clindamycin erythro minocycline	APAG **NOTE: Resistant to vancomycin**
Listeria monocytogenes	AMP	TMP/SMX	Erythro penicillin G (high dose) APAG may be synergistic with β-lactams **Cephalosporin-resistant!**
Moraxella (Branhamella) catarrhalis	AM/CL or O Ceph 2/3 TMP/SMX	Azithro clarithro dirithromycin telithro	Erythro doxy FQs
Mycoplasma pneumoniae	Erythro azithro clarithro dirithro or FQ	Doxy	(Clindamycin and β lactams NOT effective)
Neisseria gonorrhoeae (gonococcus)	Ceftriaxone, cefixime[NUS] cefpodoxime	Ofloxacin & other FQs *(Table 1, page 15)* spectinomycin	Kanamycin (used in Asia) FQ resistance in Asia rare in U S *(MMWR 47 405 1998)*
Neisseria meningitidis (meningococcus)	Penicillin G	Ceftriaxone cefuroxime cefotaxime	Sulfonamide (some strains) chloramphenicol Chloro-resistant strains found in SE Asia *(NEJM 339 868 1998)* (Prophylaxis *page 6*)
Nocardia asteroides	TMP/SMX sulfonamides (high dose)	Minocycline	Amikacin + (IMP or ceftriaxone or cefuroxime) for brain abscess
Nocardia brasiliensis	TMP/SMX sulfonamides (high dose)	AM/CL	Amikacin + ceftriaxone
Pasteurella multocida	Pen G AMP amox	Doxy AM/CL P Ceph 2 TMP/SMX	Ceftriaxone cefpodoxime FQ (active in vitro) azithro (active in vitro) *(DMID 30 99, 1998 AAC 43 1475 1999)*
Plesiomonas shigelloides	CIP	TMP/SMX	AM/CL P Ceph 1 2 3 4 IMP MER tetracycline aztreonam
Proteus mirabilis (indole–)	AMP	TMP/SMX	Most agents except nafcillin/oxacillin β lactamase (including ESBL) production now being described in P mirabilis *(JCM 40 1549 2002)*
vulgaris (indole +)	P Ceph 3 or FQ	APAG	CARB aztreonam BL/BLI
Providencia sp	Amikacin or P Ceph 3 or FQ	TMP/SMX	AP Pen + amikacin IMP
Pseudomonas aeruginosa	AP Pen AP Ceph 3 IMP MER tobramycin CIP aztreonam For serious inf use AP β-lactam + tobramycin or CIP	For UTI single drugs usually effective AP Pen AP Ceph 3 cefepime IMP MER APAG CIP aztreonam	Resistance to β-lactams (IMP ceftaz) may emerge during rx β-lactam inhibitor adds nothing to activity of TC or PIP against P aeruginosa Clavulanic acid has been shown to antagonize TC in vitro *(AAC 43 882 1999) (See also Table 5)*

TABLE 2 (3)

BACTERIAL SPECIES	ANTIMICROBIAL AGENT *(See footnote[2] for abbreviations)*		
	RECOMMENDED	ALTERNATIVE	ALSO EFFECTIVE[1] (COMMENTS)
Rhodococcus (C. equi)	IMP APAG erythro vancomycin or RIF (consider 2 agents)	CIP (variable) [resistant strains SE Asia *(CID 27 370 1998)*] TMP/SMX tetracycline or clindamycin	Vancomycin active in vitro but intracellular location of R equi may impair efficacy *(Sem Resp Inf 12 57, 1997, CID 34 1379 2002)*
Rickettsiae species	Doxy	Chloramphenicol	FQ clari azithro effective for Mediterranean spotted fever in children *(CID 34 154, 2002)*
Salmonella typhi	FQ ceftriaxone	Chloramphenicol amox TMP/SMX azithro (for uncomplicated disease *AAC 43 1441 1999*)	Multi drug resistant strains (chloramphenicol AMP TMP/SMX) common in many developing countries seen in immigrants FQ resistance now being reported *(AJTMH 61 163, 1999)*
Serratia marcescens	P Ceph 3 ERTA IMP MER, FQ	Aztreonam gentamicin	TC/CL PIP/TZ
Shigella sp.	FQ or azithro	TMP/SMX and AMP (resistance common in Middle East Latin America) Azithro rel *AnIM 126 697, 1997*	
Staph. aureus, methicillin-susceptible	Oxacillin/nafcillin	P Ceph 1 vancomycin clindamycin	Erta IMP MER, BL/BLI FQ, erythro, clarithro dirithromycin azithro quinu/dalfo, linezolid
Staph aureus methicillin-resistant	Vancomycin	Teicoplanin[NUS] TMP/SMX (some strains resistant) quinu/dalfo linezolid daptomycin	Fusidic acid[NUS] >60% CIP-resistant in U S (Fosfomycin + RIF) novobiocin Partially vancomycin-resistant strains isolated *(MMWR 27 624, 1997)*
Staph aureus methicillin-resistant [community-acquired (CA-MRSA)]			CA-MRSA usually not multiply-resistant *(Ln 359 1819 2002 JAMA 286 1201 2001)* Often resist to erythro & variably to FQ Vanco teico[NUS] or daptomycin can be used in pts requiring hospitalization
Mild moderate infection	(TMP/SMX or doxy) ± RIF	Clinda (if susceptible to erythro & clinda)	
Severe infection	Vanco or teico[NUS]	Linezolid or daptomycin	
Staph. epidermidis	Vancomycin ± RIF	RIF + (TMP/SMX or FQ)	Cephalothin or nafcillin/oxacillin if sensitive to nafcillin/oxacillin but 75% are resistant FQs *(See Table 5)*
Staph haemolyticus	TMP/SMX FQ nitro furantoin	Oral cephalosporin	Recommendations apply to UTI only
Staph lugdunensis	Oxacillin/nafcillin or penicillin G (if β-lactamase neg) *(Inf Dis Alert 22 193 2003)*	P Ceph 1 or vancomycin or teico[NUS]	Approx 75% are penicillin-susceptible Usually susceptible to gentamicin RIF *(AAC 32 2434 1990)*
Staph saprophyticus (UTI)	Oral cephalosporin or AM/CL	FQ	Susceptible to most agents used for UTI occ failure of sulfonamides nitrofurantoin reported *(JID 155 170, 1987)* Resistant to fosfomycin
Stenotrophomonas (Xanthomonas Pseudomonas) maltophilia	TMP/SMX	TC/CL or (aztreonam + TC/CL) *(AAC 41 2612 1997)*	Minocycline doxy ceftaz [In vitro synergy (TC/CL + TMP/SMX) and (TC/CL + CIP) *AAC 39 2220, 1995 CMR 11 57 1998]*
Streptobacillus moniliformis	Penicillin G or doxy	Erythro clindamycin	
Streptococcus anaerobic (Peptostreptococcus)	Penicillin G	Clindamycin	Erythro doxy vancomycin
Streptococcus pneumoniae penicillin susceptible	Penicillin G	Multiple agents effective e g amox	*See footnote, page 4*
penicillin-resistant (MIC ≥2 0)	(Vancomycin ± RIF) or (Gati Levo or Moxi) *See footnote page 4 and Table 5 page 54)*		For non-meningeal infections P Ceph 3/4 CARB quinu/dalfo, linezolid
Streptococcus pyogenes, Groups A B C G F **Strep. milleri** (constellatus intermedius anginosus)	Penicillin G or V (some add gentamicin for serious Group B strep infections & some add clinda for serious invasive Group A strep infections) *(S Med J 96 968,2003)*	All ß lactams erythro azithro dirithromycin clarithro telithro	Macrolide resistance increasing
Vibrio cholerae	Doxy FQ	TMP/SMX	Strain 0139 is resistant to TMP/SMX
Vibrio parahemolyticus	Antibiotic rx does not ↓ course		Sensitive in vitro to FQ doxy
Vibrio vulnificus alginolyticus damsela	Doxy + ceftaz	Cetotaxime FQ (e g levo *AAC 46 3580 2002)*	APAG often used in combination with ceftaz
Yersinia enterocolitica	TMP/SMX or FQ	P Ceph 3 or APAG	*CID 19 655, 1994*
Yersinia pestis (plague)	*See Table 1B page 46*		

[1] These agents are more variable in effectiveness than the Recommended or Alternative Selection of Alternative[1] or [2]Also Effective agents is based on in vitro susceptibility testing pharmacokinetics host factors such as auditory renal hepatic function and cost

[2] **AM/CL** amoxicillin clavulanate **Amox** amoxicillin **AMP** ampicillin **AM/SB** ampicillin sulbactam **APAG** antipseudomonal aminoglycosides **AP Pen** antipseudomonal penicillin *(see page 51)* **Azithro** azithromycin **BL/BLI** β lactam/β lactamase inhibitor (AM/CL TC/CL AM/SB or PIP/TZ) **CARB** carbapenems (ertapenem imipenem or meropenem) **Ceftaz** ceftazidime **CIP** ciprofloxacin **Clarithro** clarithromycin **Clinda** clindamycin **Olrithro** dirithromycin **OOT group** B distasonis B ovatus B thetaiotaomicron **Ooxy** doxycycline **ERTA** ertapenem **Erythro** erythromycin **FQ** fluoroquinolones (ciprofloxacin ofloxacin lomefloxacin enoxacin pefloxacin levofloxacin) **Gati** gatifloxacin **IMP** imipenem + cilastatin **Levo** levofloxacin **MER** meropenem **Moxi** moxifloxacin **NUS** not available in the U S **P Ceph** parenteral cephalosporins **PIP/TZ** piperacillin/tazobactam **Quinu/dalfo** quinupristin/dalfopristin **R** resistant **RIF** rifampin **TC/CL** ticarcillin clavulanate **Teico** teicoplanin **Telithro** telithromycin **TMP/SMX** trimethoprim/sulfamethoxazole **Vanco** vancomycin

TABLE 3: SUGGESTED DURATION OF ANTIBIOTIC THERAPY IN IMMUNOCOMPETENT PATIENTS[1,2]

CLINICAL SITUATION		DURATION OF THERAPY (Days)
SITE	**CLINICAL DIAGNOSIS**	
Bacteremia	Bacteremia with removable focus (no endocarditis)	10–14 *(Clin Inf Dis 14 75 1992) (See Table 1)*
Bone	Osteomyelitis adult, acute	42
	adult chronic	Until ESR[6] normal (often > 3 months)
	child acute staph and enterobacteriaceae[3]	21
	child acute strep meningococci hemophilus[3]	14
Ear	Otitis media with effusion	<2 yrs 10 (or 1 dose ceftriaxone) ≥2 yrs 5–7
	Recent meta-analysis suggests 3 days of azithro *(JAC 52 469 2003)* or 5 days of short-acting antibiotics effective for uncomplicated otitis media *(JAMA 279 1736 1998)* but may be inadequate for severe disease *(NEJM 347 1169 2002)*	
Endocardium	Infective endocarditis native valve	
	Viridans strep	14 or 28 *(See Table 1, pages 18–19)*
	Enterococci	28 or 42 *(See Table 1 page 19)*
	Staph aureus	14 (R-sided only) or 28 *(See Table 1 pages 19–20)*
Gastrointestinal *Also see Table 1*	Bacillary dysentery (shigellosis)/traveler s diarrhea	3
	Typhoid fever (S typhi) Azithro	5 (children/adolescents)
	Ceftriaxone	14*
	FQ[6]	5–7
	Chloramphenicol	14
		*[Short courses less effective *(AAC 44 450 2000)*]
	Helicobacter pylori	10–14
	Pseudomembranous enterocolitis (C difficile)	10
Genital	Non-gonococcal urethritis or mucopurulent cervicitis	7 days doxy[6] or single dose azithro[6]
	Pelvic inflammatory disease	14
Heart	Pericarditis (purulent)	28
Joint	Septic arthritis (non-gonococcal) Adult	14–28 *(Ln 351 197 1998)*
	Infant/child	Rx as osteomyelitis above
	Gonococcal arthritis/disseminated GC infection	7 *(See Table 1, page 15)*
Kidney	Cystitis (bladder bacteriuria)	3
	Pyelonephritis	14 (7 days if CIP used)
	Recurrent (failure after 14 days rx)	42
Lung	Pneumonia pneumococcal	Until afebrile 3–5 days (minimum 5 days)
	Pneumonia enterobacteriaceae or pseudomonal	21 often up to 42
	Pneumonia staphylococcal	21–28
	Pneumocystis carinii in AIDS	21
	other immunocompromised	14
	Legionella, mycoplasma, chlamydia	14–21
	Lung abscess	Usually 28–42[4]
Meninges[5] *(CID 39 1267, 2004)*	N meningitidis	7
	H influenzae	7
	S pneumoniae	10–14
	Listeria meningoencephalitis gp B strep, coliforms	21 (longer in immunocompromised)
Multiple systems	Brucellosis *(See Table 1, page 40)*	42 (add SM[6] or GM[6] for 1st 7–14 days)
	Tularemia *(See Table 1, pages 30, 40)*	7–14
Muscle	Gas gangrene (clostridial)	10
Pharynx *Also see Pharyngitis Table 1, page 32*	Group A strep pharyngitis	10 (O Ceph 2/3 azithromycin effective at 5 d) *(JAC 45, Topic TI 23 2000)* 3 d less effective *(Inf Med 18 515 2001)*
	Diphtheria (membranous)	7–14
	Carrier	7
Prostate	Chronic prostatitis (TMP/SMX)[6]	30–90
	(FQ)	28–42
Sinuses	Acute sinusitis	10–14[7]
Skin	Cellulitis	Until 3 d after acute inflammation disappears
Systemic	Lyme disease	*See Table 1, page 39*
	Rocky Mountain spotted fever *(See Table 1 page 39)*	Until afebrile 2 days

[1] It has been shown that early change from parenteral to oral regimens (about 72 hours) is cost-effective with many infections i e intra-abdominal *(AJM 91 462 1991)*

[2] The recommended duration is a minimum or average time and should not be construed as absolute

[3] These times are with proviso sx & signs resolve within 7 days and ESR[6] is normalized *(J D Nelson APID 6 59 1991)*

[4] After patient afebrile 4-5 days change to oral therapy

[5] In children relapses seldom occur until 3 days or more after termination of rx Practice of observing in hospital for 1 or 2 days after rx is expensive and non-productive For meningitis in children *see Table 1 page 4*

[6] **Azithro** = azithromycin **CIP** = ciprofloxacin **Doxy** = doxycycline **ESR** = erythrocyte sedimentation rate **FQ** = fluoroquinolones **GM** = gentamicin **rx** = treatment **SM** = streptomycin **TMP/SMX** = trimethoprim/sulfamethoxazole

[7] If pt not sx free at 10 d sinus puncture and/or rx for 7 more days *(NEJM 326 319 1992)* One study reports 3 days of TMP/SMX effective *(JAMA 273 1015 1995)* Therapy with azithro for 3 & 6 days as effective as 10 days of AM/CL *(AAC 47 2770, 2003)*

TABLE 4
COMPARISON OF ANTIMICROBIAL SPECTRA*
(These are generalizations; there are major differences between countries, areas and hospitals depending upon antibiotic usage patterns—verify for individual location. See Table 5 for resistant bacteria)

Organisms	PENICILLINS, CARBAPENEMS, AZTREONAM, FLUOROQUINOLONES																				
			Anti-staphylococcal Penicillins			Amino-Penicillins			Anti-Pseudomonal Penicillins								Fluoroquinolones							
	Penicillin G	Penicillin V	Methicillin	Nafcillin/Oxacillin	Cloxacillin/Dicloxacillin	Amp/Amox	Amox/Clav	Amp/Sulb	Ticarcillin	Ticar/Clav	Pip/Tazo	Piperacillin	Ertapenem	Imipenam	Meropenem	Aztreonam	Ciprofloxacin	Ofloxacin	Lomefloxacin	Pefloxacin[PLUS]	Levofloxacin	Moxifloxacin	Gemifloxacin	Gatifloxacin
GRAM-POSITIVE:																								
Strep Group A B C G	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	±	±	0	0	+	+	+	+
Strep pneumoniae	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	±	±	0	0	+	+	+	+
Viridans strep	±	±	±	±	±	±	±	±	±	±	±	±	+	+	+	0	0	0			+	+	+	+
Strep milleri	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	0	0			+	+	+	+
Enterococcus faecalis	+	+	0	0	0	+	+	+	±	±	+	+	±	+	±	0	**	**		0	+	+		+
Enterococcus faecium	±	±	0	0	0	+	+	+	±	±	±	±	0	±	0	0	0	0		0	0	±		±
Staph. aureus (MSSA)	0	0	+	+	+	0	+	+	0	+	+	0	+	+	+	0	+	+	+	+	+	+	+	+
Staph. aureus (MRSA)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	±		±
Staph epidermidis	0	0	±	±	±	±	+	+	±	±	+	0	+	+	+	0	+	+	+	+	+	+		+
C jeikeium	0	0	0	0	0	0	0	0	0	0		0	0	0		0	0	0						
L. monocytogenes	+	0	0	0	0	+		+	+			+	±	+	+	0	+							
GRAM-NEGATIVE:																								
N gonorrhoeae	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
N. meningitidis	+	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+	+		+
M catarrhalis	0	0	0	0	0	0	+	+	0	+	+	±	+	+	+	+	+	+	+	+	+	+		+
H influenzae	0	0	0	0	0	±	+	+	±	+	+	±	+	+	+	+	+	+	+	+	+	+		+
E. coli	0	0	0	0	0	+	+	+	±	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Klebsiella sp	0	0	0	0	0	0	+	+	0	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Enterobacter sp	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Serratia sp	0	0	0	0	0	0	0	0	+	+	+	0	+	+	+	+	+	+	+	+	+	+		+
Salmonella sp	0	0	0	0	0	±	+	+	+	+		+	+	+	+		+	+		+	+	+		+
Shigella sp	0	0	0	0	0	±	+	+	+			+	+	+	+	+	+	+		+	+	+		+
Proteus mirabilis	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Proteus vulgaris	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Providencia sp	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Morganella sp	0	0	0	0	0	±	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Citrobacter sp	0	0	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+	+		+
Aeromonas sp	0	0	0	0	0	0	+	+	+	+	+	+	+	+	+	+	+	+	+		+	+		+
Acinetobacter sp	0	0	0	0	0	0	0	+	0	+	+	0	±	+	+	0	±	±			±	±		±
Ps. aeruginosa	0	0	0	0	0	0	0	0	+	+	+	+	±	+	+	+	+	±	±		±	±		±
B (Ps.) cepacia[§]	0	0	0	0	0	0	0	0	0				0	0	+	0	0	0	0			0		0
S (X.) maltophilia[§]	0	0	0	0	0	0	0	0		±	±	±	0	0	0	0	0	0	0	0	±	+		
Y enterocolitica	0	0	0	0	0	0	±	±	±	+		+		+		+	+	+	+	+	+	+		+
Legionella sp.	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+		+	+	+		+
P multocida	+	+	0	0	0	+	+	+	+	+		+	+	+		+	+	+		+	+	+		+
H ducreyi	+					0	+	+																
MISC.:																								
Chlamydia sp	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	+	+	+		+
M. pneumoniae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	+			+	+		+
ANAEROBES:																								
Actinomyces	+	±	0	0	0	+	+	+				+	+	+		0	0	±			+			+
Bacteroides fragilis	0	±	0	0	0	0	+	+	0	+	+	0	+	+	+	0	0	0	0	0	0	±		±
P melaninogenica[§]	+	0	0	0	0	+	+	+	+	+	+	+	+	+	+	0	0	±	0		+	+		+
Clostridium difficile	+[1]							+[1]				+[1]	+[1]	+[1]	+[1]	0	0		0		0	±[1]		±[1]
Clostridium *(not difficile)*	+	+				+	+	+	+	+	+	+	+	+	+	0	±	±	0		+	+		+
Peptostreptococcus sp	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	±	±	0		+	+		+

+ =usually affective clinically or >60% suaceptible; ± = clinical trials lacking or 30–60% suaceptible; 0 = not affective clinically or <30% suaceptible; blank = data not available

§ B. melaninogenicus → Prevotella melaninogenica Pseudomonas cepacia → Burkholderia cepacia Xanthomonas → Stenotrophomonas

** Most strains ± can be used in UTI not in systemic infection

Ticar/Clav = ticarcillin clavulanate **Amp/Sulb** = ampicillin sulbactam **Amox/Clav** = amoxicillin clavulanate **MSSA** = methicillin-sensitive Staph aureus **MRSA** = methicillin resistant Staph aureus **Pip/Tazo** = piperacillin/tazobactam

[1] No clinical evidence that penicillins or fluoroquinolones are effective for C difficile enterocolitis (but they may cover this organism in mixed intra-abdominal and pelvic infections)

TABLE 4 (2)

Organisms	CEPHALOSPORINS																
	1st Generation	2nd Generation			3rd/4th Generation					Oral Agents: 1st Generation		2nd Generation			3rd Generation		
	Cefazolin	Cefotetan	Cefoxitin	Cefuroxime	Cefotaxime	Ceftizoxime	Ceftriaxone	Ceftazidime	Cefepime	Cefadroxil	Cephalexin	Cefaclor/Loracarbef*	Cefprozil	Cefuroxime axetil	Cefixime[NUS]	Ceftibuten	Cefpodox[3]/Ceftdinir/Cefditoren
GRAM-POSITIVE:																	
Strep Group A B C G	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Strep pneumoniae[1]	+	+	+	+	+	+	+	+[1]	+	+	+	+	+	+	+	±	+
Viridans strep	+	+	+	+	+	+	+	±[1]	+	+	+	+	0	+	+	0	+
Enterococcus faecalis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Staph. aureus (MSSA)	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**±**	**+**	**+**	**+**	**+**	**+**	**+**	**0**	**0**	**+**
Staph. aureus (MRSA)	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Staph epidermidis	±	±	±	±	±	±	±	±	±	±	±	±	±	±	0	0	±
C jeikeium	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	
L. monocytogenes	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
GRAM-NEGATIVE																	
N gonorrhoeae	+	±	±	±	±	±	+	±	+	0	0	±	±	±	+	±	+
N. meningitidis	**0**	**±**	**±**	**+**	**+**	**±**	**+**	**±**	**+**	**0**	**0**	**±**	**±**	**±**	**±**	**±**	
M catarrhalis	±	+	+	+	+	+	+	+	+	0	0	±	+	+	+	+	+
H influenzae	+	+	+	+	+	+	+	+			0	+	+	+	+	+	+
E. coli	**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**		**+**	**+**	**+**	**+**	**+**	**+**	**+**	**+**
Klebsiella sp	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	
Enterobacter sp	0	±	0	±	+	+	+	+	+	0	0	0	0	0	0	±	0
Serratia sp	0	+	0	0	+	+	+	+	+	0	0	0	0	0	±	±	0
Salmonella sp.					+		+				0						
Shigella sp											0						
Proteus mirabilis	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
Proteus vulgaris	0	+	+	+	+	+	+	+	+	0	0	0	0	0	+	+	±
Providencia sp	0	+	+	0	+	+	+	+	+	0	0	0	0	+	+	+	
Morganella sp	0	+	+	±	+	+	+	+	+	0	0	0	0	±	0	0	0
C. freundii	0	0	0	0	0	0	0	0	+	0	0	0	0	0	0	0	0
C diversus	0	±	±	±	+	+	+	+	+	0	0	0	0			+	
Citrobacter sp	0	±	±	±	+	+	+	+	+		0	±	0	±	+	+	+
Aeromonas sp	0	+	±	+	+	+	+	+	+						+	+	
Acinetobacter sp	0	0	0	0	+	+	+	+	±	0	0	0	0	0	0	0	
Ps. aeruginosa	**0**	**0**	**0**	**0**	**±**	**±**	**±**	**+**	**+**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
B (Ps.) cepacia[3]	0	0	0	0	±	±	±	+	±	0	0	0	0	0	0	+	
S (X.) maltophilia[3]	0	0	0	0	0	0	0	±	0	0	0	0	0	0	0	0	
Y enterocolitica	0	±	±	±	+	+	+	+	+						+	+	
Legionella sp.	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**		**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
P multocida						+	+				0				+		+
H ducreyi			+		+	+	+	+							+		
ANAEROBES:																	
Actinomyces						+	+										
Bacteroides fragilis	**0**	**±**[2]	**+**	**0**	**0**	**±**	**0**	**0**	**0**		**0**	**0**	**0**	**0**	**0**	**0**	
P melaninogenica[3]		+	+	+	+	+	±	+	0			+	+	+	+		
Clostridium difficile			**0**		**0**	**0**			**0**								
Clostridium *(not difficile)*		**+**	**+**	**+**	**+**	**+**	**+**	**+**					**+**	**+**	**0**		
Peptostreptococcus sp		+	+	+	+	+	+	+	+		-	+	+	-	+		

+ = usually effective clinically or >60% susceptible; ± = clinical trials lacking or 30–60% susceptible; 0 = not effective clinically or <30% susceptible; blank = data not available

[3] B. melaninogenicus → Prevotella melaninogenica, P. cepacia → Burkholderia cepacia. Xanthomonas → Stenotrophomonas.

* A 1-carbacephem best classified as a cephalosporin.

[1] Ceftaz 8–16x less active than cefotax/ceftriax; effective only vs Pen sens. strains *(AAC 39:2193, 1995)*. Oral cefuroxime, cefprozil, cefpodoxime most active in vitro vs resistant S. pneumo *(PIDJ 14:1037, 1995)*.

[2] Cefotetan is less active against B. ovatus, B. distasonis, B. thetaiotaomicron.

[3] **Cefpodox** = Cefpodoxime proxetil.

MSSA = methicillin-sensitive Staph. aureus. **MRSA** = methicillin-resistant Staph. aureus.

TABLE 4 (3)

Organisms	AMINOGLYCOSIDES						MACROLIDES			Ketolide	TETRACYCLINES		GLYCOPEPTIDES				URINARY TRACT AGTS		MISCELLANEOUS				
	Gentamicin	Tobramycin	Amikacin	Netilmicin[HUS]	Chloramphenicol	Clindamycin	Erythro/Dirithro	Azithromycin	Clarithromycin	Telithromycin	Doxycycline	Minocycline	Vancomycin	Teicoplanin	Fusidic Acid[HUS]	Trimethoprim	TMP/SMX	Nitrofurantoin	Fosfomycin	Rifampin	Metronidazole	Quinupristin/dalfopristin	Linezolid	Daptomycin	Colistimethate (Colistin)
GRAM-POSITIVE:																								
Strep Group A B C G	0	0	0	0	+	+	+	+	+	+	±	+	+	+	±	+	+[2]	+		+	0	+	+	+	0
Strep pneumoniae	0	0	0	0	+	+	+	+	+	+	+	+	+	+	±	±	+	+		+	0	+	+	+	0
Enterococcus faecalis	S	S	S	S	±	0	0	0	0	±	0	0	+	+	+	+	+[2]	+	+	±	0	0	+	+	0
Enterococcus faecium	S	0	0	0	±	0	0	0	0	0	0	0	±	±		0	0	+	±	0	0	+	+	+	0
Staph.aureus(MSSA)	+	+	+	+	±	+	±	+	+	+	±	+	+	+	+	±	+	+		+	0	+	+	+	0
Staph.aureus(MRSA)	0	0	0	0	0	0	0	0	0	0	±	±	+	+	+	±	+	0		+	0	+	+	+	0
Staph epidermidis	±	±	±	±	0	0	±	0	0	0	0	0	+	±	+	+	±			+	0	+	+	+	0
C jeikeium	0	0	0	0	0	0	0	0	0	0	0	0	+	+	+	0	0	0		+	0	+	+	+	0
L. monocytogenes	S	S	S	S	+		+	+	+	+	+	+	+	+		+	+			+	0	+	+	+	0
GRAM-NEGATIVE:																									
N gonorrhoeae	0	0	0	0	+	0	±	±	±		±	±	0		+	0	±	+	+	+	0	+			0
N. meningitidis	0	0	0	0	+	0	+	+		+	+	+	0	0	+	±	+			+	0	0	0		0
M catarrhalis[1]	+	+	+	+	+	0	+	+	+	+	+	+					+			+	0	+	±		
H influenzae	+	+	+	+	+	0	±	+	+	+	+	+				±	±			+	0	±	±		
Aeromonas	0				+						+	+		0			+			0	0				
E coli	+	+	+	+	+	0	0	0	0	0	+	+	0	0	0	+	+	+	+	0	0	0	0	0	+
Klebsiella sp	+	+	+	+	±	0	0	0	0	0	±	±	0	0	0	+	+	±	±	0	0	0	0	0	+
Enterobacter sp	+	+	+	+	0	0	0	0	0	0	0	±	0	0	0	±	+	±	±	0	0	0	0	0	+
Salmonella sp					+	0	0	±	0	0	±	±	0	0	0	±	+	+		0	0	0	0	0	
Shigella sp	+	+	+	+	+	0	0	±	0	0	±	±	0	0	0	±	+	+		0	0	0	0	0	
Serratia marcescens	+	+	+	+	0	0	0	0	0	0	0	0	0	0	0	0	±	0	±	0	0	0	0	0	
Proteus vulgaris	+	+	+	+	±	0	0	0	0	0	0	0	0	0	0	0	±	0	±	0	0	0	0	0	
Acinetobacter sp	0	+	0			0	0	0	0	0	0	0	0	0	0	0	0			0	0	0	0	0	+
Ps. aeruginosa	+	+	+	+	0	0	0	0	0	0	0	±	0	0	0	0	0	0		0	0	0	0	0	+
B (Ps) cepacia[3]	0	0	0	0	+	0	0	0	0	0	0	±	0	0	0	+	+	0		0	0	0	0	0	0
S (X) maltophilia[4]	0	0	0	0	+	0	0	0	0	0	0	0	0		0	0	+	0			0	0	0		
Y enterocolitica	+	+	+		+	0	0	0	0	0	0	0			0		+				0	0	0		
F tularensis	+				+						+						+			+	0	0	0		
Brucella sp	+				+	0	0	0	0	0	+	+	0	0		+	+			+	0	0			
Legionella sp.							+	+	+	+	+	+			±	+	+				0				
H ducreyi					+	+	+	+					0				±				0				
V vulnificus	±	±	±		+						+	+			0						0				
MISC.:																									
Chlamydophila sp	0	0	0	0	+	±	+	+	+	+	+	+			0	0		0		+	0	+	+		
M. pneumoniae	0	0	0	0	+	0	+	+	+	+	+	+			0						0	+	0		
Rickettsia sp	0	0	0	0	+		±			+	+	+	0	0	0						0				
Mycobacterium avium			+					+	+												0	0	0		
ANAEROBES:																									
Actinomyces	0	0	0	0	+	+	+	+	+		+	+	+		+						0				
Bacteroides fragilis	0	0	0	0	+	+	0	0	0		±	±	0			+	0				+		±		
P melaninogenica[1]	0	0	0	0	+	+		+	+		+	+	0		+						+	+			
Clostridium difficile	0	0	0	0	±								+	+							+	±	±		
Clostridium *(not difficile)***					+		±	+	+		+	+	+	+	+						+	+	+		
Peptostreptococcus sp	0	0	0	0	+	+	±	+	±	+	+	+	+	+	+						+		+		

+ = usually affective clinically or >60% suaceptible; ± = clinical triale lecking or 30–60% suaceptible; 0 = not effective clinically or <30% suaceptible; S = synargistic with panicillins (ampicillin); blank = data not available. Antimicrobiala such as azithromycin have high tiaaua penetration and aoma such as clarithromycin are metabolized to mora active compounda, hanca in vivo activity may exceed in vitro activity.

[1] In vitro results discrepant + in one study 0 in another *[JAC 31(Suppl C) 39 1993]*

[2] Although active in vitro TMP/SMX is not clinically effective for Group A strep pharyngitis or for infections due to E faecalis

[3] B melaninogenicus → Prevotella melaninogenica P cepacia → Burkholderia cepacia Xanthomonas → Stenotrophomonas

** Vancomycin metronidazole given po active vs C difficile IV vancomycin not effective

Dirithro = dirithromycin **Erythro** = erythromycin **TMP/SMX** = trimethoprim/sulfamethoxazole. **MSSA** = methicillin-sensitive Staph aureus **MRSA** = methicillin-resistant Staph aureus **S** = potential synergy in combination with penicillin ampicillin vancomycin or telcoplanin

TABLE 5: TREATMENT OPTIONS FOR SELECTED HIGHLY RESISTANT BACTERIA*

ORGANISM/RESISTANCE	THERAPEUTIC OPTIONS	COMMENT†
E. faecalis. Resistant to:		
Vanco + strep/gentamicin (MIC >500 µg/ml) β-lactamase neg *(JAC 40 161, 1997)*	Penicillin G or AMP (systemic infections) Nitrofurantoin fosfomycin (UTI only) Usually resistant to Synercid	Non BL+ strains of E faecalis resistant to penicillin and AMP recently described in Spain but unknown (except BL+ strains) so far in U S and elsewhere *(AAC 40 2420 1996)* Linezolid also effective in 60–70% of cases *(AnIM 138 135, 2003)* Daptomycin active in vitro *(JAC 52 123, 2003)*
Penicillin (β lactamase producers)	Vanco AM/SB	Appear susceptible to AMP and penicillin by standard in vitro methods Must use direct test for β-lactamase with chromogenic cephalosporin (nitrocefin) to identify in lab *(JCM 31 1965, 1993)* Rarely seen since early 1990s
E. faecium. Resistant to:		
Vanco and high levels (MIC >500 µg/ml) of streptomycin and gentamicin	Penicillin G or AMP (systemic infections) fosfomycin nitrofurantoin (UTI only)	For strains with pen/AMP MICs of >8 ≤64 µg/ml there is anecdotal evidence that high dose (300 mg/kg/ day) AMP rx may be effective Daptomycin active in vitro *(JAC 52 123, 2003)*
Penicillin AMP vanco & high-level resist to streptomycin and gentamicin *(NEJM 342 710, 2000)*	Linezolid 600 mg po or IV q12h and quinu/ dalfo 7 5 mg/ kg IV q8h are bacteriostatic against most strains of E faecium Can try combinations of cell wall-active antibiotics with other agents (including FQ chloramphenicol, RIF or doxy) Chloramphenicol alone effective in some cases of bacteremia *(CMI 7 17 2001)* Nitrofurantoin or fosfomycin may work for UTI	For strains with Van B phenotype (vanco R teico S) teicoplanin[NUS] preferably in combination with streptomycin or gentamicin If not highly AG resistant may be effective Synercid roughly 70% effective in clinical trials *(CID 30 790 2000 & 33 1816 2001)* Linezolid shows similar efficacy Comparable but somewhat lower (58% linezolid 43% QD) response rates in cancer pts *(JAC 53 646, 2004)* Emergence of resistance with therapeutic failure has occurred during monotherapy with either quinu/dalfo or linezolid *(CID 30 790 2000 Ln 357 1179 2001)* Nosocomial spread of linezolid-resistant E faecium possible *(NEJM 346 867 2002)* Daptomycin active in vitro against most strains *(JAC 52 123 2003)* **Infectious disease consultation imperative!**
S. aureus. Resistant to:		
Methicillin *(Ln 349 1901 1997 Clin Micro Rev 10 781, 1997 CID 32 108 2001)*	Vanco	Other alternatives include teicoplanin[NUS] linezolid *(Chest 124 1789 2003)* TMP/SMX (test susceptibility first) minocycline & doxy (some strains), daptomycin, or quinu/dalfo *(CID 34 1481 2002)* Fusidic acid[NUS] fosfomycin RIF novobiocin FQ may be active but must be used in combination regimens to prevent in vivo emergence of resistance Staphylococci (incl CA-MRSA) with inducible MLS_B resistance may appear susceptible to clindamycin in vitro Clinda therapy of such infections may result in therapeutic failure *(CID 37 1257 2003)* Always test for inducible resistance [easily done in lab with double-disc (D test)] before treating with clinda *(J Clin Micro 42 2777 2004)* **Investigational drugs with activity against MRSA include oritavancin (LY333328),** and **dalbavancin.**
Vanco, methicillin (VRMRSA) *(NEJM 339 520, 1998 CID 32 108, 2001 MMWR 51 902 2002 NEJM 348 1342 2003)*	Unknown but even high dose vanco may fail Linezolid quinu/ dalfo daptomycin active in vitro	Most clinical isolates of VRMRSA have had only low levels (MIC ≤16 µg/ml) of vanco resistance *(MMWR 27 624 1997 JAC 40 135 1997)* Some call these strains VISA or GISA Only anecdotal data on therapeutic regimens Most susceptible to TMP/SMX minocycline doxycycline RIF and AGs *(CID 32 108 2001)* RIF should always be combined with a 2nd therapeutic agent to prevent emergence of RIF resistance during therapy 3 clinical isolates of truly vancomycin-resistant (MIC >64) MRSA described Organisms still susceptible to TMP/SMX, chloro linezolid, minocycline, quinu/dalfo *(MMWR 51 902, 2002 NEJM 348 1342 2003)*
S. epidermidis. Resistant to:		
Methicillin	Vanco (+ RIF and gentamicin for prosthetic valve endocarditis)	
Methicillin glycopeptides	Quinu/dalfo *(see comments on E. faecium)* generally active in vitro as are linezolid & daptomycin	Vanco more active than teicoplanin[NUS] *(Clin Microbiol Rev 8 585 1995)* New FQs (levofloxacin gatifloxacin, moxifloxacin) active in vitro but development of resistance is a potential problem
S. pneumoniae. Resistant to:		
Penicillin G (MIC >0 1 ≤1 0)	Ceftriaxone or cefotaxime High-dose penicillin (≥10 million units/day) or AMP (amox) likely effective for nonmeningeal sites of infection (e g pneumonia)	IMP ERTA, cetepime cefpodoxime cefuroxime also active *(IDCP 3 75 1994)* MER less active than IMP *(AAC 38 898, 1994)* Gati gemi levo, moxi also have good activity *(AAC 38 898 1994 DMID 31 45 1998 Exp Opin Invest Drugs 8 123 1999)*
Penicillin G (MIC ≥2 0)	(Vanco ± RIF) Alternatives if non meningeal infection ceftriax/cetotax high dose AMP ERTA IMP MER or an active FQ Gati Gemi Levo, Moxi	High-dose cefotaxime (300 mg/kg/day max 24 gm/day) effective in meningitis due to strains with cefotaxime MICs as high as 2 µg/ml *(AAC 40 218, 1996)* Review *IDCP 6(Suppl 2) S21 1997*
Penicillin erythro tetracycline chloram phenicol TMP/SMX	Vanco ± RIF	60–80% of strains susceptible to clindamycin *(Diag Microbial Inf Dis 25 201, 1996)* Levo Gemi Gati Moxi active in vitro *(AAC 40 2431, 1996)*

* *Footnotes on next page*

TABLE 5 (2)

ORGANISM/RESISTANCE	THERAPEUTIC OPTIONS	COMMENT[1]
Acinetobacter baumannii. Resistant to: IMP AP Ceph 3 AP Pen APAG, FQ	AM/SB (sulbactam alone is active against some A baumannii *JAC 42 793, 1998)*)	6/8 patients with A. baumannii meningitis (7 organisms resistant to IMP) cured with AM/SB *(CID 24 932, 1997)* Various combinations of FQs and AGs IMP and AGs or AP Pens or AP Ceph 3s with AGs may show activity against **some** multiresistant strains *(AAC 41 881, 1997 AAC 41 1073, 1997 CID 36 1268, 2003)* IV colistin also effective *(CID 28 1008, 1999 CID 36 1111, 2003)* MER + sulbactam active in vitro & in vivo *(JAC 53 393, 2004)* & triple drug combinations of polymyxin B, IMP, & RIF active in vitro *(AAC 48 753, 2004)*
Campylobacter jejuni. Resistant to: FQs	Erythro azithro clarithro doxy clindamycin	Strains resistant to **both** FQs & macrolides have been reported from Thailand *(CID 22 868, 1996)* & elsewhere *(EID 7 24, 2002, AAC 47 2358, 2003)*
Klebsiella pneumoniae (producing ESBL)		
Resistant to: Ceftazidime P Ceph 3 aztreonam	IMP MER ERTA *(CID 39 31, 2004) (See Comment)*	P Ceph 4 TC/CL PIP/TZ show in vitro activity but have not been proven entirely effective in animal models *(IJAA 8 37, 1997)* and some strains which hyperproduce ESBLs are primarily resistant to TC/CL and PIP/TZ *(JCM 34 358, 1996)* Note that there are strains of ESBL-producing klebsiella for which in vitro tests suggest susceptibility to P Ceph 2, 3 but resistance to ceftazidime Infections due to such strains do not respond to P Ceph 2 or 3 *(JCM 39 2206, 2001)* FQ may be effective if susceptible Note emergence of Klebsiella sp with carbapenem resistance due to class A carbapenemase Some of these organisms resistant to all antimicrobials except colistin *(CID 39 55, 2004)*
Pseudomonas aeruginosa. Resistant to: IMP, MER	CIP (check susceptibility) APAG (check susceptibility)	Many strains remain susceptible to aztreonam & ceftazidime or AP Pens *(JAC 36 1037, 1995)* Combinations of (AP Pen & APAG) or (AP Ceph 3 + APAG) may show in vitro activity *(AAC 39 2411, 1995)* IV colistin may have some utility *(CID 28 1008, 1999)*

[1] Guideline on prevention of resistance *CID 25 584, 1997* **Abbreviations: AGs** = aminoglycosides **Amox** = amoxicillin **AMP** = ampicillin **AM/SB** = ampicillin/sulbactam **AP Ceph 3** = third generation parenteral cephalosporin with enhanced antipseudomonal activity **AP Pen** = antipseudomonal β-lactamase susceptible penicillins **APAG** = antipseudomonal aminoglycosidic antibiotics **Azithro** = azithromycin **BL** = beta lactamase **CIP** = ciprofloxacin **Clarithro** = clarithromycin **Doxy** = doxycycline **ERTA** = ertapenem **Erythro** = erythromycin **ESBLs** = extended spectrum β-lactamases **FQ** = fluoroquinolone, **Gati** = gatifloxacin **Gemi** = gemifloxacin **IMP** = imipenem cilastatin **Levo** = levofloxacin **MER** = meropenem **Moxi** = moxifloxacin **P Caph** = parenteral cephalosporin **PIP/TZ** = piperacillin/tazobactam **Quinu/dalfo** = quinupristin/dalfopristin **R** = resistant **RIF** = rifampin **S** = sensitive **TC/CL** = ticarcillin/clavulanate **Vanco** = vancomycin **VISA** = vancomycin intermediately-resistant Staph aureus **VRMRSA** = vancomycin-resistant methicillin-resistant Staph aureus

TABLE 6A: METHODS FOR PENICILLIN DESENSITIZATION

[Penicillin Allergy Reviews *CID 35 26, 2002 & MMWR 51(RR-6) 28–30 2002]*

Perform in ICU setting Discontinue all β-adrenergic antagonists Have IV line ECG and spirometer *(Curr Clin Topics Inf Dis 13 131, 1993)* Once desensitized rx must not lapse or risk of allergic reactions ↑ A history of Stevens-Johnson syndrome exfoliative dermatitis erythroderma are nearly absolute contraindications to desensitization (use only as an approach to IgE sensitivity)

Oral Route: If oral prep available and pt has functional GI tract oral route is preferred 1/3 pts will develop transient reaction during desensitization or treatment usually mild

Step *	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
Drug (mg/ml)	0 5	0 5	0 5	0 5	0 5	0 5	0 5	5 0	5 0	5 0	50	50	50	50
Amount (ml)	0 1	0 2	0 4	0 8	1 6	3 2	6 4	1 2	2 4	4 8	1 0	2 0	4 0	8 0

***** Interval between doses 15 min After Step 14, observe for 30 minutes then 1 0 gm IV

Parenteral Route:

Step **	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
Drug (mg/ml)	0 1	0 1	0 1	0 1	1 0	1 0	1 0	10	10	10	100	100	100	100	1000	1000	1000
Amount (ml)	0 1	0 2	0 4	0 8	0 16	0 32	0 64	0 12	0 24	0 48	0 1	0 2	0 4	0 8	0 16	0 32	0 64

****** Interval between doses 15 min After Step 17, observe for 30 minutes, then 1 0 gm IV

[Adapted from Sullivan TJ, in Allergy Principles and Practice Middleton, E , et al, Eds C V Mosby, 1993 p 1726, with permission]

TABLE 6B: RAPID ORAL TMP/SMX DESENSITIZATION*

Hour	Dose TMP/SMX (mg)	Comment
0	0 004/0 02	Perform in hospital or clinic Use oral suspension [40 mg TMP/200 mg SMX/5 ml (tsp)] Take 6 oz water after each dose Corticosteroids antihistaminics NOT used Refs *CID 20 849, 1995, AIDS 5 311, 1991*
1	0 04/0 2	
2	0 4/2	
3	4/20	
4	40/200	
5	160/800	

TABLE 7: RISK CATEGORIES OF ANTIMICROBICS IN PREGNANCY

DRUG	FDA PREGNANCY RISK CATEGORIES*
Antibacterial Agents	
Aminoglycosides	
Amikacin gentamicin isepamicin[NUS], netilmicin[NOS] streptomycin & tobramycin	D
Beta Lactams *(CPh 27 49, 1994)*	
Penicillins pens + BLI cephalosporins aztreonam	B
Imipenem/cilastatin	C
Meropenem, ertapenem	B
Chloramphenicol	C
Ciprofloxacin ofloxlevofloxgatifloxgemifloxmoxiflox	C
Clindamycin	B
Colistin	C
Daptomycin	B
Fosfomycin	B
Linezolid	C
Macrolides	
Erythromycins/azithromycin	B
Clarithromycin	C
Metronidazole	B
Nitrofurantoin	B
Rifaximin	C
Sulfonamides/trimethoprim	C
Telithromycin	C
Tetracyclines	D
Tinidazole	C
Vancomycin	C
Antifungal Agents: *(CID 27 1151 1998)*	
Amphotericin B preparations	B
Caspofungin	C
Fluconazole itraconazole ketoconazole flucytosine	C
Antifungal Agents: *continued))*	
Terbinafine	B
Voriconazole	D
Antiparasitic Agents:	
Albendazole/mebendazole	C
Atovaquone/proguanil	C
Chloroquine eflornithine	C
Ivermectin	C
Mefloquine	C
Miltefosine	X
Nitazoxanide	B
Pentamidine	
Praziquantel	B
Pyrimethamine/pyrisulfadoxine	C
Quinidine	C
Quinine	X
Antimycobacterial Agents:	
Capreomycin	C
Clofazimine/cycloserine	avoid [1]
Dapsone	C
Ethambutol	"safe [1]
Ethionamide	"do not use"[1]
INH pyrazinamide rifampin	C
Rifabutin	B
Rifampin	C
Thalidomide	X
Antiviral Agents:	
Abacavir	C
Acyclovir	B
Adefovir	C
Amantadine	C
Antiviral Agents: *(continued)*	
Amprenavir	C
Atazanavir	B
Cidofovir	C
Delavirdine	C
Didanosine (ddI)	B
Efavirenz	C
Emtricitabine	B
Enfuvirtide	B
Famciclovir	B
Fosamprenavir	C
Foscarnet C	C
Ganciclovir	C
Indinavir	C
Interferons	C
Lamivudine	C
Lopinavir/ritonavir	C
Nelfinavir	B
Nevirapine	C
Oseltamivir	C
Ribavirin	X
Rimantadine	C
Ritonavir	B
Saquinavir	B
Stavudine	C
Tenofovir	B
Valacyclovir	B
Valganciclovir	C
Zalcitabine	C
Zanamivir	B
Zidovudine	C

* ***FDA Pregnancy Categories:*** **A**—studies in pregnant women no risk **B**—animal studies no risk but human not adequate or animal toxicity but human studies no risk **C**—animal studies show toxicity human studies inadequate but benefit of use may exceed risk **D**—evidence of human risk, but benefits may outweigh **X**—fetal abnormalities in humans risk > benefit

Abbreviations **BLI** = ß-lactamase inhibitor **FQ** = fluoroquinolones

[1] From CDC TB Core Curriculum 3rd Ed 1994

TABLE 8: ANTIMICROBIAL AGENTS ASSOCIATED WITH PHOTOSENSITIVITY

The following drugs are known to cause photosensitivity in some individuals. There is no intent to indicate relative frequency or severity of reactions.

Source: 2004 Drug Topics Red Book, Medical Economics, Montvale, NJ. Listed in alphabetical order.

Amantadine, azithromycin, benznidazole, ciprofloxacin, clofazimine, dapsone, doxycycline, erythromycin ethyl succinate, flucytosine, ganciclovir, griseofulvin, interferons, levofloxacin, lomefloxacin, ofloxacin, pefloxacin, pyrazinamide, saquinavir, sulfonamides, tetracyclines, tretinoins, trimethoprim

TABLE 9. SELECTED PHARMACOLOGIC FEATURES OF ANTIMICROBIAL AGENTS

DRUG	DOSE, ROUTE OF ADMINISTRATION	FOR PO DOSING—Take Drug[7]			% AB[1]	PEAK SERUM LEVEL µg/ml[6]	PROTEIN BINDING, %	SERUM T½, HOURS[2]	BILIARY EXCRETION, %[3]	CSF[4]/ BLOOD, %	CSF LEVEL POTENTIALLY THERAPEUTIC[5]
		WITH FOOD	WITHOUT FOOD[8]	WITH OR WITHOUT FOOD							
PENICILLINS: Natural											
Benzathine Pen G	1 2 MU IM					0 15					
Penicillin G	2 MU IV					20	65		500	5–10	Yes for Pen-sens S pneumo
Penicillin V	500 mg po		X		60–73	5–6	65	0 5			
PEN'ASE-RESISTANT PENICILLINS											
Clox/Diclox	500 mg po		X		50	10–15	95–98	0 5			
Nafcillin/Oxacillin	500 mg po		X		Erratic	10–15	90–94	0 5	>100/25	9–20	Yes–high-dose IV therapy
AMINOPENICILLINS											
Amoxicillin	250 mg po			X	75	4–5	17	1 2	100–3000	13–14	Yes
AM/CL	875/125 mg po			X		11 6/2 2	20/30	1 4/1 1	100–3000		
AM/CL-ER		X				17/2 1	18/25	1 3/1 0			
Ampicillin	2 0 gm IV					47	18–22	1 2	100–3000	13–14	Yes
AM/SB	3 gm IV					109–150	28/38	1 2			
ANTIPSEUDOMONAL PENICILLINS											
Indanyl carb	382 mg po			X	35	6 5	50	1 0			
Piperacillin	4 gm IV					400	16–48	1 0	100–6000	30	Not for P aeruginosa marginal for coliforms
PIP/TZ	3/ 375 gm IV					209	16–48	1 0	>100		
Ticarcillin	3 0 gm IV					260	45	1 2		40	Not for P aeruginosa marginal for coliforms
TC/CL	3 1 gm IV					324	45/30	1 2			
CEPHALOSPORINS—1st Generation											
Cefadroxil	500 mg po			X	90	16	20	1 5	22		
Cefazolin	1 0 gm IV					188	73–87	1 9	29–300	1–4	No
Cephalexin	500 mg po			X	90	18–38	5–15	1 0	216		
CEPHALOSPORINS—2nd Generation											
Cefaclor	500 mg po		X		93	9 3	22–25	0 8	≥60		
Cefaclor-CD	500 mg po		X			8 4	22–25	0 8	≥60		
Cefotetan	1 0 gm IV					124	78–91	4 2	2–21		
Cefoxitin	1 0 gm IV					110	65–79	0 8	280	3	±
Cefprozil	500 mg po			X	95	10 5	36	1 5			
Cefuroxime	1 5 gm IV					100	33–50	1 5	35–80	17–88	Yes
Cefuroxime axetil	250 mg po			X	52	4 1	50	1 5			
Loracarbef			X		90	8	25	1 2			

See page 61 for all footnotes

TABLE 9 (2)

DRUG	DOSE, ROUTE OF ADMINISTRATION	FOR PO DOSING—Take Drug[7]			% AB[1]	PEAK SERUM LEVEL µg/ml[6]	PROTEIN BINDING, %	SERUM T½, HOURS[2]	BILIARY EXCRETION, %[3]	CSF[4]/ BLOOD, %	CSF LEVEL POTENTIALLY THERAPEUTIC[5]
		WITH FOOD	WITHOUT FOOD[8]	WITH OR WITHOUT FOOD							
CEPHALOSPORINS—3rd Generation											
Cefdinir pivoxil	300 mg po			X	25	1.6	60–70	1.7			
Cefditoren	400 mg po	X			16	4	88	1.6			
Cefixime[NUS]	400 mg po			X	50	3–5	65	3.1	800		
Cefotaxime	1.0 gm IV					100	30–51	1.5	15–75	10	Yes
Cefpodoxime proxetil	200 mg po	X			46	2.9	40	2.3	115		
Ceftazidime	1.0 gm IV					60	<10	1.8	13–54	20–40	Yes
Ceftibuten	400 mg po		X		80	15	65	2.4			
Ceftizoxime	1.0 gm IV					132	30	1.7	34–82		
Ceftriaxone	1.0 gm IV					150	85–95	8	200–500	8–16	Yes
CEPHALOSPORIN—4th Generation											
Cefepime	2.0 gm IV					193	20	2.0	∝5	10	Yes
CARBAPENEMS											
Ertapenem	1.0 gm IV					154	95	4	10	21	Yes
Imipenem	500 mg IV					40	15–25	1	minimal	8.5	+[9]
Meropenem	1.0 gm IV					49	2	1	3–300	Approx. 2	+
MONOBACTAM											
Aztreonam	1.0 gm IV					125	56	2	115–405	3–52	±
AMINOGLYCOSIDES											
Amikacin, gentamicin, kanamycin, tobramycin—*see Table 10C, page 72, for dose & serum levels*							0–10	2.5	10–60	0–30	No. Intrathecal 5–10 mg
Neomycin	**po**				<3	0					
FLUOROQUINOLONES[10]											
Ciprofloxacin	750 mg po			X	70	1.8–2.8	20–40	4	2800–4500		
	400 mg IV			X		4.6	20–40	4	2800–4500	26	1 µg/ml. Inadequate for Strep species *(CID 31 1131, 2000)*
	500 mg ER po			X		1.6	20–40	6.6			
	1000 mg ER po			X		3.1	20–40	6.3			
Gatifloxacin	400 mg po/IV			X	96	4.2–4.6	20	7–8		36	
Gemifloxacin	320 mg po			X	71	0.7–2.6	55–73	7			
Levofloxacin	500 mg po/IV			X	98	5.7	24–38	7		30–50	
	750 mg po/IV			X	98	8.6	24–38	7			
Moxifloxacin	400 mg po/IV			X	89	4.5	50	10–14			
Ofloxacin	400 mg po/IV			X	98	4.6/6.2	24–38	7			

See page 61 for all footnotes

TABLE 9 (3)

DRUG	DOSE, ROUTE OF ADMINISTRATION	FOR PO DOSING—Take Orug[7]			% AB[1]	PEAK SERUM LEVEL µg/ml[6]	PROTEIN BINDING, %	SERUM T½, HOURS[2]	BILIARY EXCRETION, %[3]	CSF[4]/ BLOOD, %	CSF LEVEL POTENTIALLY THERAPEUTIC[5]
		WITH FOOD	WITHOUT FOOD[8]	WITH OR WITHOUT FOOD							
MACROLIDES, AZALIDES, LINCOSAMIDES, KETOLIDES											
Azithromycin	500 mg po			X	37	0 4	7–51	68	High		
	500 mg IV					3 6	7–51	12/68			
Clarithromycin	500 mg po			X	50	3–4	65–70	5–7	7000		
	ER—500 mg po	X			∝ 50	2–3	65–70				
Dirithromycin	500 mg po	X			10	0 4	15–30	8			
Erythromycin Oral (various)	500 mg po		X		18–45	0 1–2	70–74	2–4			
Lacto/glucep	500 mg IV					3–4	70–74	2–4		2–13	No
Telithromycin	400 mg po			X	57	2 3	60–70	10			
Clindamycin	150 mg po			X	90	2 5	85–94	2 4	250–300		
	600 mg IV					10	85–94	2 4	250–300		
MISCELLANEOUS ANTIBACTERIALS											
Chloramphenicol	1 0 gm po			X	High	11–18	25–50	4 1			
Colistin	150 mg IV					5–7 5		2–3	0		No
Daptomycin	6 mg/kg IV					99	92	9			
Doxycycline	100 mg po			X		1 5–2 1	93	18	200–3200		
Fosfomycin	3 0 gm po		X			26	<10	5 7			
Linezolid	600 mg po/IV			X	100	15–20	31	5			60–70
Metronidazole	500 mg po/IV			X		20–25	20	6–14	100		
Minocycline	200 mg po			X		2 0–3 5	76	16	200–3200		
Polymyxin B	20 000 U/kg IV					1–8		4 3–6			No
Quinu/Dalfo	7 5 mg/kg IV					5		1 5			
Rifampin	600 mg po		X			4–32	80	2–5	10,000		
Rifaximin	200 mg po			X	<0 4	0 004–0 01					
Sulfamethoxazole (SMX)	2 gm po				70–90	50–120		7–12			
Trimethoprim (TMP)	100 mg po				80	1		8–15			
TMP/SMX-DS	160/800 mg po			X	85	1–2/40–60			100–200	50/40	Most meningococci resistant
	160/800 mg IV					9/105			40–70		Static vs coliforms
Tetracycline	250 mg po		X			1 5–2 2					
Vancomycin	1 0 gm IV					20–50	<10–55	4–6	50	7–14	Need high doses *See Meningitis, Table 1, page 4*
ANTIFUNGALS											
Amphotericin B											
Standard 0 4–0 7 mg/kg IV						0 5–3 5		24		0	
Ampho B lipid complex (ABLC) 5 mg/kg IV						1–2 5		24			
Ampho B cholesteryl complex 4 mg/kg IV						2 9		39			
Liposomal ampho B 5 0 mg/kg IV						58 ± 21		7–10/100			

See page 61 for all footnotes

TABLE 9 (4)

DRUG	DOSE, ROUTE OF ADMINISTRATION	FOR PO DOSING—Take Drug[7]			% AB[1]	PEAK SERUM LEVEL µg/ml[6]	PROTEIN BINDING, %	SERUM T½, HOURS[2]	BILIARY EXCRETION, %[3]	CSF[4]/BLOOD, %	CSF LEVEL POTENTIALLY THERAPEUTIC[5]
		WITH FOOD	WITHOUT FOOD[8]	WITH OR WITHOUT FOOD							
ANTIFUNGALS *(continued)*											
Caspofungin	70 mg IV x1, then 50 mg IV qd						97	9–11			
Flucytosine	2 5 gm po			X	78–90	30–40		3–6		60–100	Yes
Azoles											
Fluconazole	400 mg po/IV			X	90	6 7		20–50		50–94	Yes
	800 mg po/IV			X	90	Approx. 14		20–50			
Itraconazole	Oral soln 200 mg po		X		Low	0 3–0 7	99 8	35		0	
Voriconazole	200 mg po		X		96	3	58			22–100	Yes *(CID 37 728, 2003)*
ANTIMYCOBACTERIALS											
Ethambutol	25 mg/kg po	X			80	2–6	10–30	4		25–50	No
Isoniazid	300 mg po		X		100	3–5		0 7–4		20–90	Yes
Pyrazinamide	20–25 mg/kg po			X	95	30–50	5–10	10–16	10,000	100	Yes
Rifampin	600 mg po		X		70–90	4–32	80	1 5–5		7–56	Yes
Streptomycin	1 0 gm IV *(see Table 10C page 72)*					25–50	0–10	2 5	10–60	0–30	No Intrathecal 5–10 mg
ANTIPARASITICS											
Albendazole	400 mg po	X				0 5–1 6	70				
Atovaquone suspension	750 mg po				47	15	99 9	67		<1	No
Dapsone	100 mg po			X	100	1 1		10–50			
Ivermectin	12 mg po		X			0 05–0 08					
Mefloquine	1 25 gm po	X				0 5–1 2	98	13- 24 **days**			
Nitazoxanide	200 mg po	X				3	99				
Proguanil[11]		X					75				
Pyrimethamine	25 mg po			X	High'	0 1–0 3	87	96			
Praziquantel	20 mg/kg po	X			80	0 2–2 0		0 8–1 5			
Tinidazole	2 gm po	X			48		12	13	Chemically similar to metronidazole		
ANTIVIRAL DRUGS—NOT HIV											
Acyclovir	400 mg po			X	10–20	1 21	9–33	2 5–3 5			
Adefovir	10 mg po			X		0 02					
Famciclovir	500 mg po			X	77	3–4	<20	2–3			
Foscarnet	60 mg/kg IV					155		4		<1	No
Ganciclovir	5 mg/kg IV					8 3	1–2	3 5			
Oseltamivir	75 mg po			X	75	0 65/3 5[12]	3	1–3			
Ribavirin	600 mg po			X	64	0 8		44			
Rimantadine	100 mg po			X		0 1–0 4		25			
Valacyclovir	1000 mg po			X	55	5 6	13–18	3			
Valganciclovir	900 mg po	X			59	5 6	1–2	4			

See page 61 for all footnotes

TABLE 9 (5)

DRUG	DOSE, ROUTE OF ADMINISTRATION	FOR PO DOSING—Take Drug[7]			% AB[1]	PEAK SERUM LEVEL µg/ml[5]	PROTEIN BINDING, %	INTRACELLULAR T½, HOURS[2]	SERUM T½, HOURS[2]	CYTOCHROME P450
		WITH FOOD	WITHOUT FOOD[6]	WITH OR WITHOUT FOOD						
ANTI-HIV VIRAL DRUGS										
Abacavir	300 mg po			X	83	3 0	50	20 6	1 5	
Amprenavir	1200 mg po			X	No data	6–9	90		7–11	Inhibitor
Atazanavir	400 mg po	X			'Good	2 5	86		7	
Delavirdine	400 mg po			X	85	19 ± 11	98		5 8	Inhibitor
Didanosine	400 mg EC[13] po		X		30–40	?	<5	25–40	1 4	
Efavirenz	600 mg po		X		42	13 µM	99		52–76	Inducer/inhibitor
Emtricitabine	200 mg po			X	93	1 8	<4		10	
Enfuvirtide	90 mg sc				84	5	92		4	
Fosamprenavir	700 mg + 100 ritonavir po			X	No data	6	90	No data	7 7	
Indinavir	800 mg po		X		65	12 6 µM	60		1 2–2	Inhibitor
Lamivudine	300 mg po			X	86	2 6	<36	16	5–7	
Lopinavir	400 mg po	X			No data	9 6	98–99		5–6	Inhibitor
Nelfinavir	750 mg po	X			20–80	3–4	98		3 5–5	Inhibitor
Nevirapine	625 mg po			X	>90	2	60		25–30	Inducer
Ritonavir	300 mg po	X			65	7 8	98–99		3–5	Potent inhibitor
Saquinavir (gel)	400 mg po (with ritonavir)	X			?	?	97		1–2	Inhibitor
Stavudine	100 mg XR[14] po			X	86	1 4	"Low"	3 5	1	
Tenofovir	300 mg po	X			39	0 12	<7	10–50	17	
Zalcitabine	0 75 mg po			X	85	0 03		3	1 2	
Zidovudine	300 mg po			X	60	1–2	<38	3	1 1	

FOOTNOTES:

1. % absorbed under optimal conditions
2. Assumes CrCl >80 ml/min
3. Peak concentration in bile/peak concentration in serum x 100 If blank no data
4. CSF levels with inflammation
5. Judgment based on drug dose & organ susceptibility CSF concentration ideally ≥10 above MIC
6. Total drug, adjust for protein binding to determine free drug concentration
7. For adult oral preps not applicable for peds suspensions
8. Food decreases rate and/or extent of absorption
9. Concern over seizure potential see *Table 10*
10. Take all po FQs 2–4 hours before sucralfate or any multivalent cations Ca^{++} Fe^{++}, Zn^{++}
11. Given with atovaquone as Malarone for malaria prophylaxis
12. Oseltamivir/oseltamivir carboxylate
13. EC = enteric coated
14. XR = extended release

TABLE 9B: PHARMACODYNAMICS OF ANTIBACTERIALS*

BACTERIAL KILLING/PERSISTENT EFFECT	DRUGS	THERAPY GOAL	PK/PD MEASUREMENT
Concentration-dependent/Prolonged persistent effect	Aminoglycosides, daptomycin, ketolides, quinolones	High peak serum concentration	24-hr AUC[1]/MIC
Time-dependent/No persistent effect	Penicillins, cephalosporins, carbapenems	Long duration of exposure	Time above MIC
Time-dependent/Moderate to long persistent effect	Clindamycin, erythro/azithro/clarithro, linezolid tetracyclines, vancomycin	Enhanced amount of drug	24-hr AUC[1]/MIC

* Adapted from Craig WA IDC No Amer 17 479. 2003

[1] **AUC** = area under drug concentration curve

TABLE 10A
SELECTED ANTIBACTERIAL AGENTS—ADVERSE REACTIONS—OVERVIEW

Adverse reactions in individual patients represent all-or-none occurrences even if rare After selection of an agent the physician should read the manufacturer's package insert [statements in the product labeling (package insert) must be approved by the FDA]

Numbers = frequency of occurrence (%); + = occurs, incidence not available; ++ = significant adverse reaction; 0 = not reported; R = rare, defined as <1%. NOTE: Important reactions in bold print

ADVERSE REACTIONS	PENICILLINS, CARBAPENEMS, MONOBACTAMS, AMINOGLYCOSIDES																					
		PENICILLINASE-RESISTANT ANTI-STAPH. PENICILLINS				AMINO-PENICILLINS				AP PENS				CARBA-PENEMS				AMINO-GLYCOSIDES	MISC.	
	Penicillin G,V	Cloxacillin	Dicloxacillin	Nafcillin	Oxacillin	Amoxicillin	Amox/Clav	Ampicillin	Amp/Sulb	Piperacillin	Pip/Taz	Ticarcillin	Ticar/Clav	Ertapenem	Imipenem	Meropenem	Aztreonam	Amikacin Gentamicin Kanamycin Netilmicin[NUS] Tobramycin	Linezolid	Telithromycin
Local phlebitis	+			++	+				3	4	1	3		4	3	1	4			
Hypersensitivity	+														**3**	**3**				
Fever	+	+	+	+	+	+	+	+	+	+	2	+	+	+	+		2	+	+	
Rash	**3**	**4**	**4**	**4**	**4**	**5**	**3**	**5**	**2**	**1**	**4**	**3**	**2**	**+**	**+**	**+**	**2**			
Photosensitivity	0	0	0	0	0	0	0	0	0	0	0	0	0		0		+			
Anaphylaxis	R	0	0	R	R	0	R	R	+	0	0	+	+		+		+			
Serum sickness	4									+	+	+	+		+		+			
Hematologic																				
+ Coombs	3	0	0	R	R	+	0	+	0	+	+	0	+		2	+	R			
Neutropenia	R	0	0	+	R	+	+	+	+	6	+	0	+		+		+		1	1
Eosinophilia	+	+	+	22	22	2	+	22	22	+	+	+	5	1	+		8			
Thrombocytopenia	R	0	0	R	R	R	R	R	R	+	+	R	R		+	+	+		3–10 *(see 10B)*	
↑ PT/PTT	R	0	0	+	0	+	0	+	0	+	+	+	+		R		R			
GI																				
Nausea/vomiting		+	+	0	0	2	3	2	+	+	7	+	1	3	2	4	R		3/1	6/2
Diarrhea		+	+	0	0	5	9	10	2	2	11	3	1	6	2	5	R		4	8
C. difficile colitis		R	R	R	R	R	+	R	+	+	+	+	+		+		+		+	+
Hepatic LFTs	R	R	R	0	+	R	+	R	6	+	+	0	+	6	4	4	2		1	3
Hepatic failure	0	0	0	0	0	0	0	0	0	0	0	0	0		0					
Renal ↑ BUN, Cr	R	0	0	0	0	R	0	R	R	+	+	0	0		+	0	0	**5–25**[1]		
CNS																				
Headache	R	0	0	R	R	0	+	R	R	R	8	R	R	2	+	3	+		2	1.5
Confusion	R	0	0	R	R	0	0	R	R	R	R	R	R		+		+		+	
Seizures	R	0	0	0	+	0	R	R	0	0	R	R	+	**See footnote[2]**			+			
Special Senses																				
Ototoxicity	0	0	0	0	0	0	0	0	0	0	0	0	0		R		0	**3–14**[1]		
Vestibular	0	0	0	0	0	0	0	0	0	0	0	0	0		0		0	**4–6**[1]		
Cardiac																				
Dysrhythmias	R	0	0		0	0	0	0	0	0	0	0	0		0		+			
Miscellaneous, Unique *(Table 10B)*	+		+	+	+	+	+	+	+		+			+	+		+		+	
Drug/drug interactions, common *(Table 22)*	0	0	0	0	0	0	0	0	0	0	0	0	0		0		0	+	+	+

[1] Varies with criteria used

[2] **All β-lactams in high concentration can cause seizures** *(JAC 45 5 2000)* In rabbit IMP 10x more neurotoxic than benzylpenicillin *(JAC 22 687 1988)* In clinical trial of IMP for pediatric meningitis trial stopped due to seizures in 7/25 IMP recipients hard to interpret as purulent meningitis causes seizures *(PIDJ 10 122 1991)* Risk with IMP less with careful attention to dosage *(Epilepsia 42 1590. 2001)*

Postulated mechanism: Drug binding to $GABA_A$ receptor IMP binds with greater affinity than MER

Package insert percent seizures ertapenem 0 5, IMP 0 4 MER 0 7 However in 3 clinical trials of MER for bacterial meningitis no drug-related seizures *(Scand J Inf Dis 31 3 1999 Drug Safety 22 191, 2000)* In febrile neutropenic cancer pts IMP-related seizures reported at 2% *(CID 32 381 2001, Peds Hem Onc 17 585 2000)*

TABLE 10A (2)

ADVERSE REACTIONS	CEPHALOSPORINS/CEPHAMYCINS																				
	Cefazolin	Cefotetan	Cefoxitin	Cefuroxime	Cefotaxime	Ceftazidime	Ceftizoxime	Ceftriaxone	Cefepime	Cefpirome[NUS]	Cefaclor/Cef.ER[1]/Loracarb	Cefadroxil	Cefdinir	Cefixime[NUS]	Cefpodoxime	Cefprozil	Ceftibuten	Cefditoren pivoxil	Cefuroxime axetil	Cephalexin
Local phlebitis	+	R	R	2	5	1	4	2	1											
Hypersensitivity	5	1				2			+		2									
Fever	+	+	+			R	+	R		+	+				R	+		R	R	
Rash	+		2	R	2	2	2	2	2	1	1	+	R	1	1	1	R	R	R	1
Photosensitivity	0	0	0	0	0	R	0	0												
Anaphylaxis	R	+				R					R				R				R	
Serum sickness											<0.5[2]	+								+
Hematologic																				
Anemia				10		R					+							2	R	
+ Coombs	3	+	2	R	6	8			14	3	R							R	R	+
Neutropenia	+		2	R	+	1	+	2	1		+	+	R	R	R	R		R		3
Eosinophilia		+	3	7	1	8	4	6	1				R	R	3	2	5	R	1	9
Thrombocyto-penia	+					+	+		+		2			R	R	+	R			
↑ PT/PTT		++	+		+	+	+	+	+											
GI			2								3		3	13			6			2
Nausea/ vomiting		1		R	R	R		R	1	+	2			7	4	4	2	6/1	3	
Diarrhea		4		R	1	1		3	1	+	1-4		15	16	7	3	3	1	4	
AAC	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hepatic ↑ LFTs	+	1	3	4	1	6	4	3	+	+	3	+	1	R	4	2	R	R	2	+
Hepatic failure	0	0	0	0	0	0	0	0	0	0										
Renal ↑ BUN, Cr	+		3			R		1	+		+		R	+	4	R	R	R		+
CNS																				
Headache	0					2		R	2		3		2		1	R	R	2	R	+
Confusion	0										+					R				+
Seizures	0																			
Special Senses																				
Ototoxicity	0	0	0		0	0	0	0			0	0	0	0	0	0	0		0	0
Vestibular	0	0	0		0	0	0	0			0	0	0	0	0	0	0		0	0
Cardiac																				
Dysrhythmias	0	0	0		0	0	0	0			0	0	0	0	0	0	0		0	0
Miscellaneous, Unique *(Table 10B)*								+			+[2]							+		
Drug/drug interactions, common *(Table 22)*	0	0	0	0	0	0	0	0			0	0		0	0	0	0		0	0

[1] Cefaclor extended release tablets

[2] Serum sickness requires biotransformation of parent drug plus inherited defect in metabolism of reactive intermediates *(Ped Pharm & Therap 125 805 1994)*

* *See note at head of table page 62*

TABLE 10A (3)

ADVERSE REACTIONS (AE)	MACROLIDES			QUINOLONES[1]						OTHER AGENTS										
	Azithromycin	Clarithromycin, Reg. & ER[4]	Erythromycin	Ciprofloxacin/Cipro XR	Gatifloxacin	Gemifloxacin	Levofloxacin	Moxifloxacin	Ofloxacin	Chloramphenicol	Clindamycin	Colistimethate (Coliatin)	Daptomycin	Metronidazole	Minocycline	Quinupristin/dalfopristin[2]	Rifampin	Tetracycline/Doxycycline	TMP/SMX	Vancomycin
Rx stopped due to AE	1	3		35	29	22	4	38	4				28							
Local phlebitis					5						+		6			++		+		13
Hypersensitivity																	1	R	++	8
Fever				R	R		R			+	+	+	2				+	+	+	1
Rash	R		+	3	R	1-22[3]	17	R	2	+	+	+	4	+	+	R		+	+	3
Photosensitivity	R			R	R	R	R	R	R		4				R			+	+	0
Anaphylaxis			+	R		R	R		R											R
Serum sickness											+									
Hematologic				R														R		
Anemia										++			2						+	
Neutropenia	R	1		R	R				1	+	+			+	+			+	+	2
Eosinophilia				R					1		+				+			+	+	+
Thrombocytopenia	R	R		R						+	+			R	+			+	+	+
↑ PT/PTT		1																		0
GI			++																3	
Nausea/vomiting	3	3[5]	25	5	8/2	2.7	7/2	7/2	7		+	+	63	12	+		+		+	+
Diarrhea	5	3-6	8	2	4	3.6	1.2	6	4	+	7		5	+	+		+		3	
AAC		+	+	R	R	R	R		R		++		+				R	+		+
Hepatic LFTs	R	R	+	2	R	1.5	+		2		+					2	+	+		0
Hepatic failure	0	0															+	+		0
Renal																				
↑ BUN Cr	+	4		1					R		0		R				+	+	+	5
CNS														++						
Dizziness,lightheadedness				R	3	0.8	2.5	3	3											
Headache	R	2		1	4	1.2	5.4	2		+	+		5	+				+	+	
Confusion			+	+			+	R	2	+				+	+		+		+	
Seizures			+	+			+		R					+						
Special senses																				
Ototoxicity	+		+	0					0						+					R
Vestibular															21					
Cardiac																				
Dysrhythmias			+	R	+[3]	+[3]	+[3]	+[3]	+[3]		R									0
Miscellaneous, Unique *(Table 10B)*	+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Drug/drug interactions common *(Table 22)*	+	+	+	+	+	+	+	+	+				+			++		+	+	

[1] Concern expressed that quinolones may be associated with episodes of tendonitis
[2] Quinupristin/dalfopristin = Synercid
[3] Fluoroquinolones as class assoc **with QT_c prolongation** ↑ QT_c can cause torsades de pointes which can lead to ventricular fibrillation ↑ risk with concomitant ↓ K ↓ Mg or concomitant class Ia or IIIa antiarrhythmic agents Ref *CID 34 861, 2002*
[4] Regular and extended-release formulations
[5] Less GI upset/abnormal taste with ER formulation
[6] **Highest frequency:** females < 40 years of age after 14 d of rx

* *See note at head of table page 62*

TABLE 10B SUMMARY OF CURRENT ANTIBIOTIC DOSAGE,* SIDE-EFFECTS, AND COST§

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS *(See Table 10A for Summary)*
NATURAL PENICILLINS		**Most common adverse reactions are hypersensitivity** Anaphylaxis in up to 0.05% 5–10% fatal Commercially available skin test antigen (penicilloyl polylysine) does not predict anaphylactic reactions Hematologic renal CNS (seizures) reactions usually seen with high dose (>20 million units/day) and renal failure With procaine pen G and benzathine pen G an immediate but transient (5–30 min after injection) toxic reaction with bizarre behavior and neurologic reactions can occur (Hoigne's syndrome) Coombs test positive hemolytic anemias are rare but typically severe in contrast the Coombs test is often positive with cephalosporin therapy but clinically significant hemolysis is rare Penicillin allergy ref *JAMA 278 1895 1997*
Benzathine penicillin G (Bicillin)	**600,000–1.2 million u IM q2–4 wks** Cost 1.2 mU $66	
Penicillin G	**Low: 600,000–1.2 million u/d IM High: ≥20 million u qd IV (=12 gm)** Cost 5 mU $5.66	
Penicillin V	**0.25–0.5 gm bid, tid, qid before meals & ha** Cost 500 mg G $0.39	
PENICILLINASE-RESISTANT PENICILLINS		
Cloxacillin (Cloxapen)	**0.25–0.5 gm q6h ac, po.** Cost 250 mg G $0.70	
Dicloxacillin (Dynapen)	**0.125–0.5 gm q6h ac, po.** Cost 500 mg G $1.20	Blood levels ~2x greater than cloxacillin Acute hemorrhagic cystitis reported Acute abdominal pain with GI bleeding without antibiotic-associated colitis also reported
Flucloxacillin[NUS] (Floxapen Lutropin Staphcil)	**0.25–0.5 gm q6h po 1.0–2.0 gm q4h IV**	In Australia cholestatic hepatitis [women predominate, age >65 rx mean 2 weeks onset 3 weeks from starting rx *(Ln 339 679 1992)*] 16 deaths since 1980 recommendation use only in severe infection *(Ln 344 676, 1994)*
Nafcillin (Unipen Nafcil)	**1.0–2.0 gm q4h IV, IM.** Cost 1.0 gm $5.63	Extravasation can result in tissue necrosis With dosages of 200–300 mg/kg/d hypokalemia may occur **Reversible neutropenia (over 10% with ≥21-day rx, occasionally WBC <1000/mm³).**
Oxacillin (Prostaphlin)	**1.0–2.0 gm q4h IV, IM.** Cost 2.0 gm IV $6.53	**Hepatic dysfunction with ≥12 gm/d** LFTs usually ↑ 2–24 days after start of rx reversible ↑ SGOT in 9/11 HIV+ pts *(AnIM 120 1048 1994)* In children more rash and liver toxicity with oxacillin as compared to nafcillin *(CID 34 50 2002)*
AMINOPENICILLINS		
Amoxicillin (Amoxil Polymox)	**250 mg–1.0 gm tid po** Cost 500 mg G $0.58 NB $0.55	IV available in UK Europe IV amoxicillin rapidly converted to ampicillin Rash with infectious mono—*see Ampicillin* 500–875 mg po bid listed in past may be inadequate due to ↑ resistance
Amoxicillin/clavulanate (Augmentin) AM/CL extra-strength peds suspension AM/CL-ER—extended release adult tabs	*See Comment for adult products/cost* **Peds susp: 600/42.9 per 5 ml. Dose: 90/6.4 mg/kg div bid.** Cost 75 ml $39.00	With bid regimen less clavulanate & less diarrhea Clavulanate assoc with rare reversible cholestatic hepatitis esp men >60 yrs on rx >2 weeks *(ArIM 156 1327 1996)* 2 cases anaphylactic reaction to clavulanic acid *(J All Clin Immun 95 748 1995)* **Comparison adult Augmentin product dosega regimens:** **Cost for 10 days rx:** Augmentin 500/125 1 tab po tid $124; Augmentin 875/125 1 tab po bid $110; Augmentin XR 1000/62.5 2 tabs po bid $117
Ampicillin (Principen)	**0.25–0.5 gm q6h po.** Cost 500 mg G $0.34 **150–200 mg/kg/d IV.** Cost 1.0 gm IV G $2.80	A maculopapular rash occurs (not urticarial) **not true penicillin allergy** in 65–100% pts with infectious mono 90% with chronic lymphocytic leukemia and 15–20% with allopurinol therapy
Ampicillin/sulbactam (Unasyn)	**1.5–3.0 gm q6h IV.** Cost 3.0 gm NB $24.39 *(see Comment)*	Supplied in vials ampicillin 1.0 gm sulbactam 0.5 gm or amp 2.0 gm sulbactam 1.0 gm Antibiotic is not active vs pseudomonas Total daily dose sulbactam ≤4 gm
ANTIPSEUDOMONAL PENICILLINS NOTE: Platelet dysfunction may occur with any of the antipseudomonal penicillins esp in renal failure patients		
Piperacillin (Pipracil)	**3.0–4.0 gm q4–6h IV (200–300 mg/kg/d up to 500 mg/kg/d). For urinary tract infection: 2.0 gm q6h IV.** Cost 3.0 gm NB $12.52	1.85 mEq Na^+/gm
Piperacillin/tazobactam (Zosyn)	**3.375 gm q6h IV.** Cost 3.375 gm NB $16.52 **4.5 gm q8h available** 4.5 gm NB $20.83	Supplied as piperacillin 3.0 gm + tazobactam (TZ) 0.375 gm TZ similar to clavulanate more active than sulbactam as β-lactamase inhibitor Has ↑ activity over pip alone vs gram-negatives and anaerobes PIP/TZ 3.375 gm q6h as monotherapy **not adequate for serious pseudomones infections** For empiric or specific treatment of P aeruginosa dose is 4.5 gm IV q6h + tobramycin Rx longer than 10 d may ↑ risk of neutropenia *(CID 37 1568, 2003)* Piperacillin can cause false-pos test for galactomannan—a test for invasive aspergillosis

(See page 71 for abbreviations)

* *NOTE all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK Medical Economics*

TABLE 10B (2)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS *(See Table 10A for Summary)*
ANTIPSEUDOMONAL PENICILLINS *(continued)*		
Ticarcillin disodium (Ticar)	**3.0 gm q4–6h IV.** Cost 3 0 gm NB $13 43	Coagulation abnormalities common with large doses interferes with platelet function ↑ bleeding times may be clinically significant in pts with renal failure (4 5 mEq Na^+/gm)
Ticarcillin/clevulanate (Timentin)	**3.1 gm q4–6h IV.** Cost 3 1 gm NB $15 37	Supplied in vials ticarcillin 3 0 gm, clavulanate 0 1 gm/vial 4 5–5 0 mEq Na^+/gm Diarrhea due to clavulanate Rare reversible cholestatic hepatitis secondary to clavulanate *(ArIM 156 1327, 1996)*
CARBAPENEMS. NOTE: In pts with pen allergy 11% had allergic reaction after imipenem or meropenem *(CID 38 1102, 2004)*		
Ertapenem (Invanz)	**1.0 gm qd IV/IM.** Cost 1 0 gm $49 97	Lidocaine diluent for IM use, ask about lidocaine allergy
Imipenem + cilastatin (Primaxin)	**0.5 gm q6h IV.** Cost 500 mg NB $33 10	For seizure comment *see footnote 2, Table 10A, page 62* In pts with history of pen allergy & pos pen skin tests ½ had pos IMP skin tests *(J All Clin Imm 82 213, 1988)* Resistance of P aeruginosa reported *(see Table 5)*
Meropenem (Merrem)	**0.5–1.0 gm q8h IV. Up to 2.0 gm q8h IV for meningitis.** Cost 1 0 gm NB $54 94	For seizure incidence comment, *see Table 10A, page 62* Comments Does not require a dehydropeptidase inhibitor (cilastatin) Activity vs aerobic gm-neg slightly ↑ over IMP activity vs staph & strep slightly ↓, anaerobes = to IMP B ovatus B distasonis more resistant to meropenem
MONOBACTAMS		
Aztreonem (Azactam)	**1.0 gm q8h–2.0 gm q6h IV.** Cost 1 0 gm NB $21 61	Can be used in pts with allergy to penicillins/cephalosporins Animal data and a letter raise concern about cross-reactivity with ceftazidime *(Rev Inf Dis 7 613, 1985)* side-chains of aztreonam and ceftazidime are identical
CEPHALOSPORINS (1st parenteral, then oral drugs).	**NOTE:** Prospective data demonstrate correlation between use of cephalosporins (esp 3rd generation) and ↑ risk of C difficile toxin-induced diarrhea May also ↑ risk of colonization with vancomycin-resistant enterococci ***For cross-allergenicity, see Oral, next page.***	
1st Generation, Parenteral		
Cefazolin (Ancef, Kefzol)	**0.25 gm q8h–1.5 gm q6h IV, IM.** Cost 1 0 gm G $2 74 NB $5 60	Do not give into lateral ventricles—seizures!
2nd Generation, Parenteral		
Cefotetan (Cetotan)	**1–3 gm q12h IV, IM. (Max. dose not >6 gm qd).** Cost 1 0 gm NB $11 90	Increasing resistance of B fragilis, Prevotella bivivus, Prevotella disiens (most common in pelvic infections) Ref *CID 35(Suppl 1) S126 2002* Methylthiotetrazole (MTT) side chain can inhibit vitamin K activation
Cefoxitin (Mefoxin)	**1.0 gm q8h–2.0 gm q4h IV, IM.** Cost 1 0 gm G $11 23, NB $15 29	In vitro may induce ↑ β-lactamase esp in Enterobacter sp clinical significance ?
Cefuroxime (Keturox Ceftin, Zinacet)	**0.75–1.5 gm q8h IV,IM.** Cost 1 5 gm IV G $23 90	More stable vs staphylococcal β-lactamase than cefazolin
3rd Generation, Parenteral	Use of P Ceph 3 drugs correlates with incidence of C difficile toxin diarrhea, perhaps due to cephalosporin resistance of C difficile *(CID 38 646, 2004)*	
Cefotaxime (Claforan)	**1.0 gm q8–12h to 2.0 gm q4h IV.** Cost 2 0 gm G $22, NB $26 38	Maximum daily dose 12 gm
Ceftazidime (Fortaz Tazicef)	**1.0–2.0 gm q8–12h IV, IM.** Cost 2 0 gm NB $28 93–43 30	Excessive use may result in ↑ incidence of C difficile-assoc diarrhea and/or selection of vancomycin-resistant E faecium Ceftaz is susceptible to extended-spectrum cephalosporinases *(CID 27 76 & 81 1998)*
Ceftizoxime (Cetizox)	**1.0 gm q8–12h to 4.0 gm q8h IV.** Cost 2 0 gm NB $24 64	Maximum daily dose 12 gm

(See page 71 for abbreviations)

* *NOTE all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK Medical Economics*

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS *(See Table 10A for Summary)*
CEPHALOSPORINS, 3rd Generation, Parenteral *(continued)*		
Ceftriaxone (Rocephin)	**Commonly used IV dosage in adults:** **< Age 65: 2.0 gm once daily** **> Age 65: 1.0 gm once daily** **Purulent meningitis: 2.0 gm q12h.** Can give **IM** in 1% lidocaine. Cost 1.0 gm NB $56.16	Dosage 2.0 gm IV qd gives better tissue levels than 1.0 gm q12h (overcomes protein binding) *(see footnote[1])* 'Pseudocholelithiasis' 2° to sludge in gallbladder by ultrasound (50%), symptomatic (9%) *(NEJM 322:1821, 1990)*. More likely with ≥2 gm/d with pt on total parenteral nutrition and not eating *(AnIM 115:712, 1991)*. Clinical significance still unclear but has led to cholecystectomy *(JID 17:356, 1995)* and gallstone pancreatitis *(Ln 17:662, 1998)*
4th Generation, Parenteral		
Cefepime (Maxipime)	**1.0–2.0 gm q12h IV.** Cost 2.0 gm NB $35.86	Active vs P. aeruginosa and many strains of Enterobacter, serratia, C. freundii resistant to ceftazidime, cefotaxime, aztreonam *(CID 20:56, 1995)*. More active vs S. aureus than 3rd generation cephalosporins.
Cefpirome[NUS] (HR 810)	**1.0–2.0 gm q12h IV**	Similar to cefepime, ↑ activity vs enterobacteriaceae, P. aeruginosa, Gm + organisms. Anaerobes: less active than cefoxitin, more active than cefotax or ceftaz.
Oral Cephalosporins		The oral cephalosporins are generally safe. **Patients with a history of IgE-mediated allergic reactions to a penicillin (e.g., anaphylaxis, angioneurotic edema, immediate urticaria) should not receive a cephalosporin.** If the history is a "measles-like" rash to a penicillin, available data suggest a 5–10% risk of rash in such patients; there is no enhanced risk of anaphylaxis. Cephalosporin skin tests, if available, predictive of reaction *(AnIM 141:16, 2004)* Any of the cephalosporins can result in **C. difficile toxin**-mediated diarrhea/enterocolitis. The reported frequency of nausea/vomiting and non-C. difficile toxin diarrhea is summarized in Table 10A. There are few drug-specific adverse effects, e.g.: ***Cefaclor*** Serum sickness-like reaction 0.1–0.5%—arthralgia, rash, erythema multiforme but no adenopathy, proteinuria or demonstrable immune complexes. Anecdotal reports of similar reaction to loracarbef. Appear due to mixture of drug biotransformation and genetic susceptibility *(Ped Pharm & Therap 125:805, 1994)* ***Cefdinir*** Drug-iron complex causes red stools in roughly 1% of pts. ***Cefditoren pivoxil*** Hydrolysis yields pivalate. Pivalate absorbed (70%) & becomes pivaloylcarnitine which is renally excreted, 39–63% **↓ in serum carnitine concentrations**. Carnitine involved in fatty acid (FA) metabolism & FA transport into mitochondria. Effect transient & reversible. No clinical events documented to date *(Med Lett 44:5, 2002)* Also contains caseinate (milk protein) **avoid if milk allergy** (not same as lactose intolerance). Need gastric acid for optimal absorption. ***Cefpodoxime*** There are rare reports of acute liver injury, bloody diarrhea, pulmonary infiltrates with eosinophilia.
1st Generation, Oral		
Cefadroxil (Duricef)	**0.5–1.0 gm q12h po.** Cost 0.5 gm G $2.48, NB $6.32	
Cephalexin (Keflex, Keftab, generic)	**0.25–0.5 gm q6h po.** Cost 0.5 gm G $0.44, NB $1.64–4.85	
2nd Generation, Oral		
Cefaclor (Ceclor)	**0.25–0.5 gm q8h po.** Cost 0.25 gm G $0.66, NB $2.46	
Cefaclor-ER (Ceclor CD)	**0.375–0.5 gm q12h po.** Cost 0.5 gm $3.50	
Cefprozil (Cefzil)	**0.25–0.5 gm q12h po.** Cost 0.5 gm NB $9.10	
Cefuroxime axetil po (Ceftin)	**0.125–0.5 gm q12h po.** Cost 0.5 gm NB $10.30	
Loracerbef (Lorabid)	**0.4 gm q12h po.** Cost 0.4 gm NB $6.37	
3rd Generation, Oral		
Cefdinir (Omnicef)	**300 mg q12h or 600 mg qd.** Cost 300 mg $4.45	
Cefditoren pivoxil (Spectracef)	**200–400 mg bid po.** Cost 200 mg $1.88	
Cefixime[NUS] (Suprax)	**0.2–0.4 gm q12–24h po.** Cost 0.4 gm NB $10.18, G $1.00	
Cefpodoxime proxetil (Vantin)	**0.1–0.2 gm q12h po.** Cost 0.2 gm NB $7.80	
Ceftibuten (Cedax)	**0.4 gm qd po.** Cost 0.4 gm NB $9.10	

AMINOGLYCOSIDES AND RELATED ANTIBIOTICS—*See Table 10C, page 72, and Table 17, page 132*

[1] The age-related dosing of ceftriaxone is based on unpublished pharmacokinetic data that show an age-related reduction in hepatic clearance of ceftriaxone; hence, there is possible underdosing in younger pts; therefore the suggested 2 gm/day dose.

(See page 71 for abbreviations)

* *NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function.* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK, Medical Economics*

TABLE 10B (4)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS *(See Table 10A for Summery)*
GLYCOPEPTIDES		
Teicoplanin[NUS] (Targocid)	**For septic arthritis—maintenance dose 12 mg/kg/ d; S. aureus endocarditis—trough serum levels >20 µg/ml required (12 mg/kg q12h x3 loading dose, then 12 mg/kg qd)**	Hypersensitivity fever (at 3 mg/kg 2.2% at 24 mg/kg 8.2%) skin reactions 2.4% Marked ↓ platelets (high dose ≥15 mg/kg/d) Red neck syndrome less common than with vancomycin *(JAC 32 792 1993)*
Vancomycin (Vancocin)	**15 mg/kg q12h IV; 125 mg q6h po; intrathecal 5–10 mg q48–72h** Cost 1.0 gm IV G $6.00 NB $16.00 Oral 'Pulvule' 125 mg Cost $7.70 For other uses **see *Comment*.** One report of safety & efficacy of once-daily vanco 30 mg/kg *(JAC 49 155 2002)*	**Measure serum levels** if planned dose ≥2.0 gm/d rapidly changing renal function chronic renal failure or on hemodialysis Target levels peak 20–50 µg/ml, trough 5–10 µg/ml Rapid infusion (over <1 hr) can cause non-specific histamine release manifest as angioneurotic edema, flushed skin ("red neck syndrome") or hypotension Can continue vanco but infuse over 1–2 hrs **Ototoxicity and nephrotoxicity now rare** unless vanco given with an aminoglycoside aminoglycoside amplifies the risk of nephrotoxicity Neutropenia rash occur Rarely association with linear IgA bullous dermatosis *(CID 38 442 2004)* **Intrathecal vanco** occ used for meningitis and/or ventriculitis/shunt infections **Initial** dosing ranges from 5–10 mg/d (infants) to 10–20 mg/d (children/adults) adjusted to achieve trough CSF conc of 10–20 µg/ml *(AnPharmacotherapy 27 912, 1993)* **Critically ill pts:** Safe & reasonable to give loading dose of 25 mg/kg at 500 mg/ hr *(JAC 47 246, 2001)*
CHLORAMPHENICOL, CLINDAMYCIN(S), ERYTHROMYCIN GROUP, KETOLIDES, OXAZOLIDINONES, QUINUPRISTIN/DALFOPRISTIN (SYNERCID)		
Chloramphenicol (Chloromycetin)	**0.25–1 gm po/IV q6h to max. of 4 gm/day** Cost 1.0 gm IV $7.60 po $2.40	No oral drug distributed in U.S. Hematologic (↓ RBC ~1/3 pts aplastic anemia 1 21 600 courses) Gray baby syndrome in premature infants anaphylactoid reactions optic atrophy or neuropathy (very rare) digital paresthesias minor disulfiram like reactions
Clindamycin (Cleocin)	**0.15–0.45 gm q6h po. 600–900 mg q8h IV, IM** Cost 300 mg po NB $5.43 G $3.76 600 mg IV NB $7.92 G $8.44	**Lincomycin** (Lincocin) 0.6 gm q8h IV IM Cost 600 mg IV $10.51 Based on number of exposed pts these drugs are the most frequent cause of **C. difficile toxin-mediated diarrhea** In most severe form can cause pseudomembranous colitis/toxic megacolon
Erythromycin Group (Review drug interactions before use) Ref *Mayo Clin Proc 74 613 1999*		**Motilin** is gastric hormone that activates duodenal/jejunal receptors to initiate peristalsis Erythro (E) and E esters both po and IV activate motilin receptors and cause uncoordinated peristalsis with resultant 20–25% incidence of anorexia nausea or vomiting *(Gut 33 397 1992)* Less binding and GI distress with azithromycin/clarithromycin Systemic erythro in 1st 2 wks of life associated with **infantile hypertrophic pyloric stenosis** *(J Peds 139 380 2001)* **Frequent drug-drug interactions** *see Table 22 page 145* Major concern is prolonged QT_c interval on EKG **Prolonged QTc:** Mutations in 6 genes (LQT 1–6) produce abnormal cardiac K^+/Na^+ channels Variable penetrance no symptoms repeated syncope to sudden death **↑ risk if female & QT_c >500 msec! Risk amplified by drugs** [macrolide antiarrhythmics & drug-drug interactions *(see FQs page 70 for list)*] Can result in torsades de pointes (ventricular tachycardia) and/or cardiac arrest Refs *NEJM 348 1837 & 1866 2003 351 1053 & 1089 2004 www.qtdrugs.org* Cholestatic hepatitis in approx 1/1000 adults (not children) given E estolate **Transient reversible tinnitus or deafness** with ≥4 gm/d of erythro IV in pts with renal or hepatic impairment Reported with ≥600 mg/d of azithro *(CID 24 76 1997)* Dosages of oral erythro preparations expressed as base equivalents With differences in absorption/biotransformation variable amounts of erythro esters required to achieve same free erythro serum level e.g. 400 mg E ethyl succinate = 250 mg E base Macrolide-induced Churg-Strauss syndrome reported in an atopic pt *(Ln 350 563 1997)* **Dirithromycin** available as once-daily macrolide **Very low serum levels; do not use if potential for bacteremic disease.**
Azithromycin (Zithromax)	**po: 0.5 gm on day 1, then 0.25 gm qd on days 2–5 po or 0.5 gm po qd x3 d** Cost 250 mg $7.85 Z-Pak $47.00 600 mg $19.00 **IV: 0.5 gm/d** Cost $27.38	
Base and esters (Erythrocin, Ilosone) IV name E lactobionate	**0.25 gm q6h–0.5 gm q6h po. IV: 15–20 mg/kg up to 4.0 gm qd. Infuse over 30 or more minutes** Cost po 250 mg base G $0.18 stearate $0.18 estolate $0.31 ES 400 $0.23 IV 1.0 gm NB $6.50	
Clarithromycin (Biaxin) or clarithro extended release (Biaxin XL)	**0.5 gm q12h po** Cost 500 mg $4.55 **Extended release: Two 0.5 gm tabs po/d** Cost 500 mg ER $4.66	
Dirithromycin (Dynabac)	**0.5 gm po qd** Cost 250 mg $4.36	
Ketolide **Telithromycin** (Ketek)	**Two 400 mg tabs po qd—anticipated dose** 400 mg tabs Cost 400 mg $5.36	1st ketolide (similar to erythro) **Common:** diarrhea 10% nausea 7% vomiting 2.4% **Uncommon: blurred vision** 2° slow accommodation occurs in 1% (women 40 y/o 2%) may cause exacerbation of **myasthenia gravis** Potential QT prolongation Several **drug-drug interactions** *(Table 22, page 147)*

(See page 71 for abbreviations)

* *NOTE all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK Medical Economics*

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS (See Table 10A for Summary)
CHLORAMPHENICOL, CLINDAMYCIN(S), ERYTHROMYCIN GROUP, KETOLIDES, OXAZOLIDINONES, QUINUPRISTIN/DALFOPRISTIN (SYNERCID) *(continued)*		
Linezolid (Zyvox)	**PO or IV dose: 600 mg q12h all indications except 400 mg q12h for uncomplicated skin infections** Available as 400 & 600 mg tabs, oral suspension (100 mg/5 ml), & IV solution. 600 mg po $62, 600 mg IV $82	**Reversible myelosuppression:** thrombocytopenia, anemia, & neutropenia reported. Most often after >2 wks of therapy. Not sure of incidence of thrombocytopenia after 2 wks of rx: 7/20 osteomyelitic pts, 5/7 pts treated with vanco & then linezolid. Refs: *CID 37:1609, 2003 & 38:1058 & 1065, 2004* **Other reported serious adverse effects:** Lactic acidosis (N/V, low HCO_3), toxic neuropathy reported after prolonged therapy (peripheral neuropathy *LnID 4:528, 2004* & optic neuropathy *JAC 53:1114, 2004*) **Inhibitor of monoamine oxidase**: risk of severe hypertension if taken with foods rich in tyramine. Be careful with drugs containing pseudoephedrine, phenylpropanolamine or if taking SSRIs.[1] **Serotonin syndrome** (fever, agitation, mental status changes, tremors) reported *(CID 36:1197, 2003 & 37:1274, 2003)*
Quinupristin + dalfopristin (Synercid)	**7.5 mg/kg q8h IV via central line** Cost: 350 mg–150 mg $122	Venous irritation (5%), none with central venous line. Asymptomatic ↑ in unconjugated bilirubin. **Arthralgia** 2%–50% *(CID 36:476, 2003)* **Drug-drug interactions:** Cyclosporine, nitedipine, midazolam, many, more—*see Table 22*
TETRACYCLINES *(Mayo Clin Proc 74:727, 1999)*		
Doxycycline (Vibramycin, Doryx, Monodox, Adoxa)	**0.1 gm po or IV q12h** Cost: 100 mg po G $0.08–0.11, NB $4.86; 100 mg IV NB $14.16	Similar to other tetracyclines. ↑ nausea on empty stomach. Erosive esophagitis, esp. if taken hs. Phototoxicity +, but less than with tetracycline. Deposition in teeth less. Can be used in patients with renal failure. *Comments:* Effective in treatment and prophylaxis for malaria, leptospirosis, typhus fevers
Minocycline (Minocin, Dynacin)	**0.1 gm q12h po** Cost: 100 mg G $1.80; NB $3.88	Similar to other tetracyclines. **Vestibular symptoms** (30–90% in some groups, none in others): vertigo 33%, ataxia 43%, nausea 50%, vomiting 3%, women more frequently than men. Hypersensitivity pneumonitis, reversible, ~34 cases reported *(BMJ 310:1520, 1995)* *Comments:* More effective than other tetracyclines vs staph and in prophylaxis of meningococcal disease. P. acnes many resistant to other tetracyclines, not to minо. Actνe vs Nocardia asteroides. Mycobacterium marinum
Tetracycline, Oxytetracycline (Sumycin)	**0.25–0.5 gm q6h po, 0.5–1.0 gm q12h IV** Cost: 250 mg po $0.06	GI (oxy 19%, tetra 4), anaphylactoid reaction (rare), deposition in teeth, negative N balance, hepatotoxicity, enamel agenesis, pseudotumor cerebri/encephalopathy. Outdated drug. Fanconi syndrome. *See drug-drug interactions, Table 22* **Contraindicated in pregnancy, hepatotoxicity in mother, transplacental to tetus.** *Comments:* IV dosage over 2.0 gm/d may be associated with fatal hepatotoxicity
FLUOROQUINOLONES (FQs)		
Ciprofloxacin (Cipro) and **Ciprofloxacin-extended release** (Cipro XR)	**500-750 mg bid po. Urinary tract infection: 250 mg bid po or Cipro XR 500 mg qd. Parenteral** rx 200–400 mg q12h IV. Cost: 500 mg po $5.80, Cipro XR 500 mg $8.66, 400 mg IV $30.00	**Children:** No FQ approved for use under age 16 based on joint cartilage injury in immature animals. Articular SEs in children est. at 2–3% *(Ln ID 3:537, 2003)* **CNS toxicity.** Poorly understood. Varies from mild (lightheadedness) to moderate (confusion) to severe (seizures). May be aggravated by NSAIDs. **Gami akin rash:** Macular rash after 8–10 d of rx. Frequency highest females < age 40 treated 14 d (22.6%). In men < age 40 treated 14 d frequency 7.7%. Mechanism unclear. Indication to DC therapy. **Hypoglycemia/hyperglycemia** *(Med Lett 45:64, 2003)*: Data based on case reports only. Various FQs ↑ insulin release in rats. No known drug interactions, most pts reported have type 2 diabetes, no interaction with oral hypoglycemic drugs found. No data to allow comparative frequency between FQs. **Opiate screen false-positives**: FQs can cause **false-positive urine assay for opiates** *(JAMA 286:3115, 2001)* **Photosensitivity** *See Table 8, page 56* ***(Continued on next page—QT_c interval prolongation & Tendinopathy)***
Gatifloxacin (Tequin)	**200–400 mg IV/po qd** Cost: 400 mg po $9.56, 400 mg IV $38.20	
Gemifloxacin (Factive)	**320 mg po qd** Cost: 320 mg $18.78	
Levofloxacin (Levaquin)	**250–750 mg qd po or IV** Cost: 750 mg po $20, 750 mg IV $58	

[1] **SSRI** = selective serotonin reuptake inhibitors, e.g., fluoxetine (Prozac)

(See page 71 for abbreviations)

* *NOTE: all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK, Medical Economics*

TABLE 10B (6)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS (See Table 10A for Summary)
FLUOROQUINOLONES *(continued)*		
Moxifloxacin (Avelox)	400 mg po or IV qd Cost 400 mg po $10 00, IV $44 00	*(Continued from previous page)* **QT$_c$ (corrected QT) interval prolongation** ↑ QT$_c$ (>500 msec or >60 msec from baseline) is considered possible with any FQ ↑ QT$_c$ can lead to torsades de pointes and ventricular fibrillation Risk low with current marketed drugs) Risk ↑ in women ↓ K$^+$ ↓ Mg bradycardia (Refs *NEJM 348 1837 & 1866 2003*) Major problem is ↑ risk with concomitant drugs **Avoid concomitant drugs with potential to prolong QT$_c$:** **Antiarrhythmics:** Amiodarone, Disopyramide, Dofetilide, Flecainide, Ibutilide, Procainamide, Quinidine, Risperidone, Sotalol; **Anti-Infectivas:** Clarithro, Erythro, Foscarnet, Mefloquine, Pentamidine; **Anti-Hypertensives:** Bepridil, Isradipine, Nicardipine, Moexipril; **CNS Drugs** Fluoxetine, Sertraline, Tricyclics, Venlataxine, Haloperidol, Phenothiazines, Pimozide, Quetiapine, Ziprasidone; **Misc.** Salmeterol, Naratriptan, Sumatriptan, Dolasetron, Droperidol, Fosphenytoin, Indapamide, Tamoxiten, Tizanidine **Updates online: www.qtdruge.org; www.torsades.org.** **Tendinopathy** Over age 60 approx 2–6% of all Achilles tendon ruptures attributable to use of FQ *(ArIM 163 1801, 2003)* ↑ risk with concomitant steroid or renal disease *(CID 36 1404, 2003)*
Ofloxacin (Floxin)	200–400 mg bid po Cost 400 mg po $6	
POLYMYXINS *(CID, in press)*		
Polymyxin B (Poly-Rx)	Rarely used parenterally in U S Use colistin for parenteral therapy	Used as/for bladder irrigation intrathecal ophthalmic Source Bedford Labs Bedford, OH
Polymyxin E = colistin Colistin sulfate used po or topical IV form is **colistimethate** (Coly-Mycin M)	1 mg colistin = 12,500 IU U S 2 5–5 0 mg/kg/d div in 2–4 equal doses U K , >60 kg 80–160 mg q8h	**Inhalation** dose 80 mg q12h **Intrathecal:** not standardized Reports range from 1 6 mg to 20 mg intraventricularly usually 10 mg **Nephrotoxicity** (tubular necrosis) Reports vary from 14–20% Reversible **Neurotoxicity** (frequency?) Vertigo facial paresthesia, abnormal vision confusion, ataxia & neuromuscular blockade → respiratory failure Dose-dependent
MISCELLANEOUS AGENTS		
Daptomycin (Cubicin) *(Med Lett 46 11, 2004 CID 38 994 2004)*	**Skin/soft tissue: 4 mg/kg qd IV** **Bacteremia/endocarditis: 6 mg/kg qd IV** *(see Comment)* Cost 500 mg $161	FDA approved skin/soft tissue infections Bacteremia/endocarditis trials ongoing **Potential muscle toxicity:** At 4 mg/kg/d ↑ CPK in 2 8% dapto pts & 1 8% comparator-treated pts In very small study no CPK ↑ in pts taking a statin drug given daptomycin (manufacturer suggests stopping statins during dapto rx)
Fosfomycin (Monurol)	**3.0 gm with water po x1 dose** Cost $35 00	Diarrhea in 9% compared to 6% of pts given nitrofurantoin and 2 3% given TMP/SMX
Fusidic acid^{Nus} (Fucidin)	**500 mg tid po, IV** *(Leo Laboratories, Denmark)*	Mild GI occ skin rash jaundice (17% with IV, 6% with po) (None in CSF <1% in urine)
Immune globulin IV therapy	**Dosage, frequency vary with the indication** At least 7 manufacturers Cost for 10–12 gm ranges from $500–$1100	Reported adverse effects range from 1–15% Fever headache myalgia N/V relate to rate of infusion mild & self-limited **More serious** anaphylactoid reactions thromboemboli aseptic meningitis & renal injury in 6 7% *(QJM 93 751, 2000)*
Methenamine hippurate (Hiprex Urex)	**1.0 gm q6h po** Cost 1 0 gm $1 49 1 0 gm = 480 mg methenamine	Nausea and vomiting skin rash or dysuria Overall ~3% Methenamine requires (pH ≤5) urine to liberate formaldehyde Useful in suppressive therapy after infecting organisms cleared do not use for pyelonephritis *Comment* Do not force fluids may dilute formaldehyde Of no value in pts with chronic Foley If urine pH >5 0 co-administer ascorbic acid (1–2 gm q4h) to acidify the urine cranberry juice (1200–4000 ml/day) has been used results ±
Methenamine mandelate (Mandelamine)	**1.0 gm q6h po (480 mg methenamine)** Cost 1 0 gm NB $0 69	

(See page 71 for abbreviations)

* *NOTE all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK Medical Economics*

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE* (Cost§)	ADVERSE REACTIONS, COMMENTS *(See Table 10A for Summary)*
MISCELLANEOUS AGENTS *(continued)*		
Metronidazole (Flagyl) Ref *Mayo Clin Proc 74 825 1999*	**Anaerobic infections: usually IV, 7.5 mg/kg (~500 mg) q6h (not to exceed 4.0 gm qd). With long T½, can use IV at 15 mg/kg q12h. If life-threatening, use loading dose of 15 mg/kg IV. Oral dose: 500 mg qid** Cost 500 mg tab G $0 21 NB $4 56 500 mg IV G $2 80 NB $26 16 70 gm vaginal gel $57 48 Ext release 750 mg $9	Can be given rectally (enema or suppository) In pts with **decompensated liver disease** (manifest by ≥2 L of ascites, encephalopathy ↑ prothrombin time, ↓ serum albumin) **t½ prolonged; unless dose ↓ by approx. ½, side-effects** ↑ Absorbed into serum from vaginal gel **Neurol.:** headache, rare paresthesias or peripheral neuropathy ataxia seizures aseptic meningitis report of reversible metro-induced cerebellar lesions *(NEJM 346 68 2002)* **Avoid alcohol during & 48 hrs after (disulfiram-like reaction)** Very dark urine (common but harmless) Skin urticaria Mutagenic in Ames test Tumorigenic in animals (high dose over lifetime) No evidence of risk in man No teratogenicity
Mupirocin (Bactroban)	**Skin cream or ointment 2%: Apply tid x10 d.** 15 gm $31 48 **Nasal ointment 2%: apply bid x5 d** 22 gm NB $47 50 G $42 70	Headache 1 7% rash & nausea 1 1%
Nitrofurantoin macrocrystals (Macrodantin Furadantin))	**100 mg q6h po** Cost 100 mg G $1 21 NB $2 15 **Dose for long-term UTI suppression: 50–100 mg at bedtime**	Absorption ↑ with meals Increased activity in acid urine much reduced at pH 8 or over Not effective in endstage renal disease *[JAC 33(Suppl A) 121 1994]* Nausea and vomiting hypersensitivity peripheral neuropathy Pulmonary reactions (with chronic rx) acute ARDS type **chronic desquamative interstitial pneumonia with fibrosis** Intrahepatic cholestasis & hepatitis similar to chronic active hepatitis Hemolytic anemia in G6PD deficiency Contraindicated in renal failure Should not be used in infants <1 month of age
monohydrate/macrocrystals (Macrobid)	**100 mg bid po** Cost 100 mg $2 26	Efficacy of Macrobid 100 mg bid = Macrodantin 50 mg qid Adverse effects 5 6% less nausea than with Macrodantin
Rifaximin (Xifaxan)	**One 200 mg tab po tid** x3 d Cost 200 mg $3 66	For traveler s diarrhea In general adverse events equal to or less than placebo
Sulfonamides [e g , sulfisoxazole (Gantrisin) sulfamethoxazole (Gantanol)]	Sulfisoxazole (Gantrisin) peds suspension Cost 500 mg/5 ml 480 ml $46 02	**Short-acting are best:** high urine concentration and good solubility at acid pH More active in alkaline urine **Allergic reactions** skin rash drug fever pruritus photosensitization Periarteritis nodosa & SLE, Stevens-Johnson syndrome serum sickness syndrome myocarditis Neurotoxicity (psychosis neuritis), hepatic toxicity Blood dyscrasias usually agranulocytosis Crystalluria Nausea & vomiting headache dizziness lassitude mental depression acidosis sulfhemoglobin Hemolytic anemia in G6PD deficient & unstable hemoglobins (Hb Zurich) Do not use in newborn infants or in women near term ↑ frequency of kernicterus (binds to albumin, blocking binding of bilirubin to albumin)
Tinidazole (Tindamax)	**2 gm po x1 with food** Cost 2 gm $18 24	**Adverse reactions:** metallic taste 3 7%, nausea 3 2%, anorexia/vomiting 1 5% All higher with multi-day dosing
Trimethoprim (Trimpex Proloprim and others)	**100 mg tab po q12h or 200 mg (2 tabs) po q24h** Cost 100 mg NB $0 90 G $0 15	Frequent side-effects are rash and pruritus Rash in 3% pts at 100 mg bid 6 7% at 200 mg qd Rare reports of photosensitivity exfoliative dermatitis Stevens-Johnson syndrome toxic epidermal necrosis and aseptic meningitis *(CID 19 431, 1994)* Check drug interaction with phenytoin Increases serum K^+ *(see TMP/SMX Comments)* TMP can ↑ homocysteine blood levels *(Ln 352 1827, 1998)*
Trimethoprim (TMP)/ Sulfamethoxazole (SMX) (Bactrim Septra) Single-strength (SS) is 80 TMP/400 SMX double-strength (DS) 160 TMP/800 SMX Ref *ArIM 163 402, 2003*	**Standard po rx (UTI, otitis media): 1 DS tablet bid. P. carinii: see *Table 13, page 96*. IV rx (base on TMP component): standard 8–10 mg/kg/d divided q6h, q8h, or q12h. For ahigeliosis: 2.5 mg/kg IV q6h** Cost 160/800 po G $0 15, NB $2 160/800 IV $11 21	Adverse reactions in 10% or more of pts GI and skin GI nausea vomiting anorexia Skin Rash, urticaria, photosensitivity Less often but more serious (1–10%) Stevens-Johnson syndrome and toxic epidermal necrolysis Skin adverse reactions may represent toxic metabolites of SMX and ↓ glutathione rather than allergy *(An Pharm 32 381, 1998)* Daily ascorbic acid 0 5–1 0 gm may promote detoxification *(J AIDS 36 1041, 2004)* TMP competes with creatinine for tubular secretion and serum creatinine can ↑ TMP also blocks distal renal tubule reabsorption of Na^+ and secretion of K^+ ↑ serum K^+ in 21% of pts *(AnIM 124 316, 1996)* TMP/SMX suspected etiology of aseptic meningitis esp TMP component *(CID 19 431 1994)* TMP/SMX contains sulfites and may trigger asthma in sulfite-sensitive pts One of most frequent drugs to cause thrombocytopenia *(AnIM 129 886 1998)*

Abbreviations: **G** = generic **NB** = name brand **MRSA** = methicillin-resistant Staph aureus **APAG** = antipseudomonal aminoglycoside **NUS** = not available in the U S

* *NOTE all dosage recommendations are for adults (unless otherwise indicated) & assume normal renal function* § *Cost = average wholesale price from 2004 DRUG TOPICS RED BOOK Medical Economics*

TABLE 10C
AMINOGLYCOSIDE ONCE-DAILY AND MULTIPLE DAILY DOSING REGIMENS
(See Table 17, page 132, if estimated creatinine clearance <90 ml/min.)

General: Dosage given as both once-daily (OD) and multiple daily dose (MDD) regimens.

Pertinent formulae (1) Estimated creatinine clearance (CrCl) $\frac{(140-\text{age})(\text{ideal body weight in kg})}{(72)(\text{serum creatinine})^{\dagger}}$ = CrCl for men in ml/min multiply answer x 0.85 for CrCl of women

(2) Ideal body weight (IBW)—Females 45.5 kg + 2.3 kg per inch over 5' = weight in kg
Males 50.0 kg + 2.3 kg per inch over 5 = weight in kg

(3) Obesity adjustment use if actual body weight (ABW) is ≥30% above IBW. To calculate adjusted dosing weight in kg IBW + 0.4(ABW–IBW) = adjusted weight *(CID 25:112, 1997)*

DRUG	MDD AND OD IV REGIMENS/ TARGETED PEAK (P) AND TROUGH (T) SERUM LEVELS	COST[§] Name Brand (NB), Generic (G)	COMMENTS For more data on once-daily dosing, see *AJM 105:182, 1998, and Table 17, page 132*
Gantamicin (Garamycin) **Tobramycin** (Nebcin)	MDD 2 mg/kg load then 1.7 mg/kg q8h P 4–10 µg/ml T 1–2 µg/ml OD 5.1 (7 if critically ill) mg/kg q24h P 16–24 µg/ml, T <1 µg/ml	Gentamicin 80 mg $5.75 Tobramycin 80 mg NB $7.28, G $11.96	**All aminoglycosides have potential to cause tubular necrosis and renal failure, deafness due to cochlear toxicity, vertigo due to damage to vestibular organs, and rarely neuromuscular blockade.** Risk minimal with oral or topical application due to small % absorption unless tissues altered by disease Risk of nephrotoxicity ↑ with concomitant administration of cyclosporine vancomycin ampho B radiocontrast Risk of nephrotoxicity ↓ by concomitant AP Pen and perhaps by once-daily dosing method (especially if baseline renal function normal) In general same factors influence risk of ototoxicity **NOTE: There is no known method to eliminate risk of aminoglycoside nephro/ototoxicity. Proper rx attempts to ↓ the % risk.** The clinical trial data of OD aminoglycosides have been reviewed extensively by meta-analysis *(CID 24:816, 1997)* **Serum levels:** Collect serum for a peak serum level (PSL) exactly 1 hr after the start of the infusion of the 3rd dose. In critically ill pts it is reasonable to measure the PSL after the 1st dose as well as later doses as volume of distribution and renal function may change rapidly Other dosing methods and references. For once-daily 7 mg/kg/d of gentamicin—Hartford Hospital method *see AAC 39:650, 1995*
Kanamycin (Kantrex) **Amikacin** (Amikin) Streptomycin	MDD 7.5 mg/kg q12h P 15–30 µg/ml T 5–10 µg/ml OD 15 mg/kg q24h P 56–64 µg/ml T <1 µg/ml	Kanamycin 1.0 gm $6.92 Amikacin 500 mg NB $34.26 G $7.80 Streptomycin 1.0 gm $9.75	
Netilmicin[NUS]	MDD 2.0 mg/kg q8h P 4–10 µg/ml T 1.2 µg/ml OD 6.5 mg/kg q24h P 22–30 µg/ml T <1 µg/ml		
Isepamicin[NUS]	Only OD Severe infections 15 mg/kg q24h less severe 8 mg/kg q24h		
Spectinomycin (Trobicin)	2.0 gm IM x1—gonococcal infections	2 gm NB $29.76	
Neomycin oral	Prophylaxis GI surgery 1.0 gm po x3 with erythro.. *see Table 15B page 124* For hepatic coma 4–12 gm/d po	500 mg G $1.24	
Tobramycin—inhaled (Tobi) *See Cystic fibrosis Table 1 page 29* Adverse effects few transient voice alteration (13%) and transient tinnitus (3%) Cost 300 mg $54.46			
Paromomycin– oral *See Entamoeba and Cryptosporidia Table 13 page 93* Cost 250 mg $1.90			

† Estimated CrCl invalid if serum creatinine <0.6 mg/dl Consultation suggested

§ *Cost average wholesale price from 2004 DRUG TOPICS RED BOOK Medical Economics*

TABLE 11A: TREATMENT OF FUNGAL, ACTINOMYCOTIC, AND NOCARDIAL INFECTIONS—ANTIMICROBIAL AGENTS OF CHOICE*

(See Table 11B for Amphotericin B Preparations and Adverse Effects)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Actinomycosis *(CID 26 1255 1998)* (A israelii most common also A naeslundii A viscosus A odontolyticus A meyeri A gerencseriae) Cervicofacial pulmonary abdominal cerebral & rarely pericarditis *(ID Clin Prac 12 233 2004)*	**Ampicillin** 50 mg/kg/d IV x 4–6 wks then 0.5 gm **amoxicillin** tid po **OR Penicillin G** 10–20 million u/d IV x 4–6 wks then **penicillin V** 2–4 gm/d po Duration can likely be individualized esp with surgical debulking, total duration 3–6 mos usually adequate for thoracic & abdominal & 3–6 wks for cervicofacial *(CID 38 444, 2004)*	**Doxycycline** or **ceftriaxone** or **clindamycin** or **erythromycin** **Chloramphenicol** 12.5–15 mg/kg IV/po q6h has been recommended for CNS infection in pen-allergic pts	Tuboovarian abscesses may complicate IUDs. Removal of IUD is primary rx. With abscesses or fistulae, surgery often required. While penicillin G and ampicillin IV have been effective with home IV therapy agents given qd, e.g., ceftriaxone, are more practical *(CID 19 161 1994)* **Surgery may be necessary for hemoptysis** *(Am Thor Surg 74 185, 2002)*
Aspergillosis (A. fumigatus most common, also A. flavus and others) *(CID 30 696, 2000)*			
Allergic bronchopulmonary aspergillosis (ABPA) ABPA found in 1–2% of pts with asthma & 1–15% with cystic fibrosis *[CID 37 (Suppl 3) 37, 2003]* Clinical manifestations: wheezing, pulmonary infiltrates, bronchiectasis & fibrosis. Airway colonization assoc with ↑ blood eosinophils, ↑ serum IgE, ↑ specific serum IgE & IgG antibodies	Acute asthma attacks associated with ABPA **Corticosteroids**	Rx of ABPA: **Itraconazole**[1] 200 mg po qd x16 wks or longer	In 2 PRCTs[2], itra ↓ number of exacerbations requiring corticosteroids (p <0.03), improved immunological markers (eosinophils in sputum & ↓ serum IgE levels) & in 1 study improved lung function & exercise tolerance *(NEJM 342 756, 2000; Cochrane Database Syst Rev 3 CD001108, 2004)*. Itra improved 21 cystic fibrosis pts with ABPA *(Allergy 57 723, 2002)*. [For rx of ABPA in CF, *see CID 37(Suppl 3) 225, 2003*]
Allergic fungal sinusitis relapsing chronic sinusitis, nasal polyps without bony invasion, asthma, eczema or allergic rhinitis, ↑ IgE levels and isolation of Aspergillus sp. or other dematiaceous sp. (Alternaria, Cladosporium, etc.)	**Rx controversial:** systemic corticosteroids + surgical debridement (80% respond but 2/3 relapse)	For failures might try **itra**[1] 200 mg po bid x12 mos. *(CID 31 203, 2000)*	In 1 report, fungal elements identified by histopathology in up to 93% of cases of 'chronic sinusitis' & in a randomized, double-blind, placebo-controlled trial in 24 pts, intranasal ampho was assoc. with a ↓ in mucosal thickening of 8.8% by CT scan vs ↑ of 2.5% in placebo. Nasal inflammation score ↓ by 70% vs placebo *(LnID 4 257, 2004)*. Controversial area, need more data
Aspergilloma (fungus ball) *(J Resp Dis 23 300, 2002)*	Efficacy of antimicrobial agents not proven. **Itraconazole** (po) of benefit in 10/14 pts *(J Am Acad Derm 23 607, 1990)*. Another case responded to itra 200 mg/d x3 mos. *(IDCP 7 122, 1998)*		Surgery if hemoptysis becomes massive (post-op complications 25%)
Invasive, pulmonary (IPA) or extrapulmonary: Occurs post-transplantation and post chemotherapy in neutropenic pts (PMN <500/mm³). Most common pneumonia in stem cell transplant recipients with graft vs host disease *(CID 35 659, 2002)*. Usually a late (≥100 days) complication in allogeneic bone marrow & liver transplantation, median survival 36 days, but **overall mortality rates vary from 78–94%** *(CID 28 322, 1999; CID 36 46, 2003)*	**Voriconazole** 6 mg/kg IV q12h on day 1, then either (4 mg/kg IV q12h) or (200 mg po q12h for body weight ≥40 kg, but 100 mg po q12h for body weight <40 kg) **OR** **Lipid-based ampho B** may be as effective and less nephrotoxic than standard ampho B **but much more expensive** *(see footnote[1] page 75 for dosages)*. Some authorities now prefer lipid-based ampho B over standard ampho B as initial rx *(CID 32 415, 2003)* **OR** **Ampho B** *(see footnote[2] page 74)*. Rapid increase to 1 mg/kg (1–1.25 mg/kg if neutropenic) qd IV. Total dose of 2–2.5 gm rec. by some but data to support this lacking. **OR** **Combination rx: Vori** *(in above dosages)* + **caspo** *(dosage below)* are currently preferred initial treatment in many bone marrow transplant units, esp. in pts receiving high doses of corticosteroids **Alternative: Caspofungin** 70 mg IV on day 1, then 50 mg IV qd (reduce to 35 mg with moderate hepatic insufficiency) For all regimens, if response good may switch to oral **vori** after 2–3 wks	**Voriconazole** more effective than ampho B in one large randomized trial of 277 immunosuppressed pts with IPA, 53% responded vs 32% rx with ampho B. Overall survival better (71 vs 58%) *(NEJM 347 408, 2002)*. Appears particularly advantageous in cerebral aspergillosis *[EJCMID 22 297, 2003; AnHematol 83(Suppl 1) 542, 2004]* & as salvage rx in those with refractory infection *(Eur J Haematol 73 50, 2004; PIDJ 23 584, 2004)*. However, 12/139 stem cell transplant (SCT) pts treated with vori had breakthrough fungal infections (6 zygomyces) with more resistant (MIC >1 µg/ml to vori) isolates *(CID 39 743, 2004)* **Ampho B overall success rate 34–42%** *(CID 26 781, 1998; 32 358, 2001)* in pulmonary aspergillosis in those pts rx ≥14 days. Success dependent on underlying disease: 83% heart/kidney transplants, 54% neutropenic leukemia pts, 33% bone marrow transplant, 20% liver transplant *(CID 23 608, 1996)*. **A. terreus infections particularly resistant to ampho B: in 83 cases, 73.4% mortality with ampho B rx vs 55.8% with voriconazole rx (p <0.01)** *(CID 39 192, 2004)*. **Use vori!** **Caspofungin.** FDA approval based on 50% response in 40 pts who received >7 days of rx *(ICAAC 2000, Abst. 1103)*. In 83 pts reported to date, overall efficacy rate was 45% but was 56% in those receiving >7 days of caspofungin as salvage rx *(ICAAC 2002, Abst. M-856)*. 42% with hematological malignancies had favorable response but only 14% with allogenic stem cell transplants. Failure of resolution of neutropenia predicted rx failure. Minimal toxicity reported *(Transpl Inf Dis 1 25, 2002)*. **Combination antifungal rx** (*CID 36 1445, 2003*). While new drugs may ↑ response & survival, IPA remains one of the most refractory fungal infections. This has led clinicians to combination rx albeit **to data no controlled clinical trials have been reported to support this approach**. Antagonism between the 3 classes of drugs does not seem to exist & synergism between the triazoles (vori and itra) + echinocandins (caspo) *(AAC 47 1416, 2003)* and ampho B (incl. lipid-based) + caspo *(AAC 46 245, 2002)* is demonstrated in vitro & in neutropenic animal models *(AAC 46 2564, 2002; JID 187 1834, 2003)*. Case reports & small uncontrolled series reported in pts who

(continued on next page)

[1] **Oral solution preferred to tablets because of ↑ absorption** *(see Table 11B, page 83)*

[2] **PRCTs** = Prospective randomized controlled trials

See page 81 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

TABLE 11A (2)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE PRIMARY	ANTIMICROBIAL AGENTS OF CHOICE ALTERNATIVE	COMMENTS
Aspergillosis/Invasive, pulmonary (IPA) or extrapulmonary: *(continued)* *(continued from previous page)* IA attractive *(JID 190 441 2004 CID 39 199 2004)* **False-pos. tests consistently found in serum from pts receiving PIP/TZ** *(CID 38 913 & 917, 2004, NEJM 349 24 2003)* Test available at MiraVista 1-866-647-2847	*(See previous page)*	*(continued from previous page)* have failed conventional ampho B rx >100 pts have either had caspo added to ampho B-based regimen or had vori & caspo substituted for ampho B with an overall response rate of approx 50% *(ICAAC 2002, Abst M-859 860 1820, Cancer 97 1025 2003 AnHematol 83 390 2004)* In a retrospective series of bone marrow transplant pts who failed short-course ampho B vori + caspo was superior to vori alone *(CID 39 797 2004)* Randomized trials needed *(CID 39 803 2004)* Toxicity of the vori & caspo is low high cost is the major deterrent to combination rx Unfortunately already variants of A fumigatus isolated from 7 stem cell transplant pts who received itra showed ↓ susceptibility to itra vori, caspo, & 2/7 ampho B *(AAC 48 1197, 2004)*	
Blastomycosis *(CID 30 679, 2000)* (Blastomyces dermatitidis) Cutaneous pulmonary or extrapulmonary	**Itraconazole**[3] oral solution 200–400 mg/d po for 6 mos **OR Ampho B**[2] 0 7–1 mg/kg/ d to a total dose of ≥1 5 gm for very sick pts	**Fluconazole** 400–800 mg/d for at least 6 mos 85%+ effective for non-life-threatening disease *(CID 25 200 1997)*	Itra in patients treated for ≥2 months 95% cure *(AJM 93 489 1992)* Ampho B successful in >90% when ≥1 5 gm total dose used *(CID 22 S102 1996)* For blood/urine antigen call 1-866 647-2847

Candidiasis A decrease in C albicans and increase in non-albicans species show ↓ susceptibility to antifungal agents (esp fluconazole) These changes have predominantly affected immunocompromised pts in environments where antifungal prophylaxis (esp fluconazole) is widely used *(JAC 49 (Suppl 1) 3, 2002 PIDJ 23 635 & 687 2004)* In vitro susceptibility testing for antifungal drugs to date has not undergone rigorous in vivo validation studies and clinical outcomes are often more dependent on host factors *(Am J Med 112 380 2002)* Yet it seems prudent to use susceptibility profiles to help select empiric antifungal therapy The table summarizes current published reports of frequency of candida isolates, and interpretation as to whether a drug is clinically effective **(S = susceptible)** may require dose escalation **(S-DD = suaceptible with dosa aacalation)**, or is likely to be ineffective **(R = resistant)** *(Ln 359 1135, 2002)* **S-I = less activity in vitro but clinically effective** only rare failures reported *(IDSA Guidelines 2004 CID 38 161, 2004)* In vitro testing for caspo not standardized

	% of Candida Isolates	Risk Factors	% Sensitive In Vitro Fluconazole	Itraconazole	Voriconazole	Ampho B	Caspofungin	Rx if species known
C albicans	41–65	HIV/AIDS surgery	97% (S)	93% (S)	99% (S)	>95% (S)	S	Flu [++] caspo or ampho B
C glabrata	10–15	Heme malignancies, azole prophylaxis	85–90% (S-DD)	50% (R)	92% (S-I)	>95% (S-I)	S	Caspo, ampho B or vori
C parapsilosis	15–24	Azole prophylaxis, neonates, foreign bodies	99% (S)	4% (S DD)	99% (S)	>95% (S)	S-I	Flu, caspo or ampho B
C tropicalis	5–10	Neutropenia	98% (S)	58% (S)	99% (S)	>95% (S)	S	Flu, caspo, or ampho B
C krusei	2–10	Heme malignancies, azole prophylaxis	5% (R)	69% (R)	99% (S-I)	>95% (S-I)	S	Caspo ampho B or vori
C guilliermondi	1	Azole prophylaxis previous ampho rx	>95% (S)	? (S)	>95% (S)	? (R)	S	Flu caspo or vori
C lusitaniae	1	Previous ampho rx	>95% (S)	? (S)	>95% (S)	? (R)	S	Flu caspo, or vori

[++] If patient had prior heavy basal exposure use ampho B or caspo *(CID 35 1073 2002, 36 1497 2003)*

Bloodstream: clinically stable with or without venous catheter *(IDSA Guidelines CID 38 161 2004)*

- **All positive blood cultures require therapy!**
- Remove & replace venous catheter (not over a wire) if possible *(CID 34 591 & 600 2002 36 1221, 2003)* esp in non-neutropenic mortality 21% vs 4% if catheter not removed
- Ophthalmologic exam recommended for all pts with candidemia
- Treat for 2 wks after last pos blood culture & resolution of signs & symptoms of infection

Fluconazole ≥6 mg/kg/d or 400 mg qd IV or po x7 d then po for 14 d after last + blood culture **OR Caspofungin** 70 mg IV on day 1 followed by 50 mg IV qd (reduce to 35 mg IV qd with moderate hepatic insufficiency) Would use in place of flu in those heavily pretreated with azoles (i e flu or itra prophylaxis) **OR Ampho B** 0 6 mg/kg qd IV, total dose 5–7 mg/kg or lipid-based ampho B[4]

In pts who fail to respond or deteriorate higher doses of either drug may be used (**ampho B** 0 8–1 mg/kg/d IV or **fluconazole** 800 mg/d IV or po) *(CID 25 43, 1997)* **Be sure catheter is removed.**

or

Voriconazole[NFDA-I]: loading dose 6 mg/kg q12h x1 d. IV, then maintenance dose 3 mg/kg q12h IV for serious candida infections

Observational studies suggest flu & ampho B are similarly effective in neutropenic pts *(IDSA Guidelines 2003)*

A randomized study (277 pts 10% were neutropenic) found caspofungin equivalent to ampho B (0 6–1 mg/kg/d) for invasive candidiasis For candidemia 71 7% rx with caspo vs 62 8% with ampho B had successful outcomes but caspo had significantly less toxicity *(NEJM 347 2020 2002)*

[1] **Dosages: ABLC** 5 mg/kg/d IV over 2 hrs **Ampho B cholesteryl complex** 3–4 mg/kg/d IV given as 1 mg/kg/hr **liposomal Ampho B** 3–5 mg/kg/d IV given over 1–2 hrs

[2] Hydration before and after infusion with 500 cc saline has been shown to reduce renal toxicity

[3] **Oral solution preferred to tablets because of ↑ absorption** *(see Table 11B page 83)*

[4] ABLC or liposomal ampho B recommended for pts intolerant of or refractory to ampho B i e failure of 500 mg ampho B initial renal insufficiency (creatinine >2 5 mg/dl or CrCl < 25 ml/min)

* From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is average wholesale price (AWP).**

See page 81 for abbreviations All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (3)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Candidosis *(continued)*			
Bloodstream: unstable, deteriorating ± neutropenia OR stable disseminated (pulmonary, eye, hepatosplenic) *(IDSA Guidelines CID 38 161 2004)* *For endophthalmitis, see below*	**Ampho B** 0 8–1 mg/kg/d IV ± 5FC 37 5' mg/kg po q6h or **lipid-based ampho B** (ABLC) 5 mg/kg/d **OR** **Fluconazole** 400–800 mg (or >6 mg/kg/d) qd IV It start ampho B switch to flucon 400 mg po qd x14 d after last positive blood culture resolution of neutropenia & disappearance of signs/ symptoms of candidal infection **OR** **Combination of fluconazole** 800 mg/d + **ampho B** 0 7 mg/kg/d for first 5–6 days then switch to flu 400 mg/d po	**Voriconazole** loading dose 6 mg/kg q12h x1 d IV then maintenance dose 3 mg/kg q12h IV for serious candida infections or **Caspofungin** 70 mg IV on day 1 followed by 50 mg IV qd (reduce to 35 mg IV qd with moderate hepatic insufficiency)	In a randomized trial of 219 pts with non neutropenic candidemia fluconazole (800 mg/d) + ampho B (0 7 mg/kg/d for the 1st 5 days) was slightly better than flu alone Primary analysis success rate on day 30 was 69% vs 57% (p= 08) respectively overall success rate 69% vs 56% (p= 045) and clearance of fungemia 94% vs 83% (p= 02) The flu alone group were slightly sicker (APACHE 15 0 vs 16 8 p= 039) and renal toxicity in combination greater (23% vs 3% p < 001) *(CID 36 1221, 2003)* Given difficulty with interpretation of this study the editors would reserve combination of flu + ampho B for only the sickest candidemic patient Voriconazole may have a role in this clinical setting *(Euro Con Clin Micro & Inf Dis 2002 Abst 237 IDSA 2002 Abst 352)*
Chronic mucocutaneous	**Ketoconazole** 400 mg/d po (as single daily dose with food) for 3–9 months	Usually children Peds dose of **fluconazole** 3–6 mg/kg/d as single daily dose	Respond to ampho B but relapse is usual Fluconazole used and may be less toxic but experience limited
Cutaneous *(including paronychia, Table 1, page 18)*	Apply topical **ampho B, clotrimazole, econazole, miconazole** or **nystatin** 3-4x daily for 7–14 days or **ketoconazole** 400 mg po once daily x14 d **Ciclopirox olemine** 1% cream/lotion Apply topically bid x7–14 d		Cost (30 gm tube cream) AB $29 Clo $13, Eco $19 MIC $21 Nys $3 58 Cic $18 20
Endocarditis Causes C albicans 24% non-albicans Candida sp 24% Aspergillus sp 24% others 27% *(CID 32 50, 2001)*	**(Ampho B** 0 6 mg/kg/d IV for 7 days then 0 8 mg/kg qod IV or **lipid-based ampho B** 3–5 mg/kg/d Continue 6–8 weeks after surgery **+ flucytosine** 25–37 5 mg/kg po qid) + surgical resection	**Fluconazole** 200–400 mg/d for chronic suppression may be of value when valve cannot be replaced *(Chest 122 302 2002)* + Surgical resection	**Adjust flucyt dose and interval to produce serum levels; peak 70–80 mg/L, trough 30–40 mg/L** With nephrotoxicity dosage of flucyt needs to be↓ Surgery may not always be required *(CID 22 262 1996, Scand J Inf Dis 32 86 2000)* Caspofungin cidal vs candida & may be of value no data Candida endocarditis has propensity to relapse requires careful follow-up for at least a year *(Chest 99 1531, 1991)*
Endophthalmitis *(IDSA Guidelines CID 38 161 2004))* • Occurs in 10% of candidemia *(PIDJ 23 635 2004)* thus ophthalmological consult for all pts • Diagnosis typical white exudates on retinal exam and/or isolation by vitrectomy	[**Ampho B** or **lipid-based ampho B** (ABLC 4 5 mg/kg/d)] **OR fluconazole** 400 mg/d IV or po either as initial rx or follow-up after ampho B Role of intravitreal ampho B not well defined but commonly used in pts with substantial vision loss *(CID 27 1130, 1998)* Treat x6–12 weeks		Treatment results mixed in several small series Fluconazole *(CID 20 657 1995)* ABLC *(J Inf 40 92 2000)*, and vitrectomy *(CID 27 1130 1998)*
Oral (thrush)—not AIDS patient *(See below for vaginitis)*	**Fluconazole** 200 mg single dose or 100 mg/d po x14 days or **Itraconazole** oral solution 200 mg (20 ml) qd without food x7 days	**Nystatin pastilles** (200 000 u) lozenge qid 500,000 u (swish & swallow) qid or 2 (500 000 u) tabs tid for 14 d **OR** **Clotrimazole** 1 troche (10 mg) 5x/d x14d	Maintenance not required in non-AIDS pts Usually improves in 3–4 days longer rx ↓ relapse Fluconazole-resistant C krusei fungemia reported in flucon-rx pts *(NEJM 325 1315, 1991)*

serum Cr (to >2 5 mg/dl for adults or 1 5 mg/dl for children) or severe acute administration-related toxicity *(CID 26 1383, 1998)* Since efficacy similar and toxicity less some now recommend lipid-based preps in place of ampho B as initial rx *(CID 32 415 2003)*

[1] Some experts reduce dose of 5FC to 25 mg/kg q6h

* From 2004 Drug Topics Red Book, Medical Economics Data and Hospital Formulary Pricing Guide **Price is average wholesale price (AWP).**

See page 81 for abbreviations *All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 11A (4)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE — PRIMARY	ANTIMICROBIAL AGENTS OF CHOICE — ALTERNATIVE	COMMENTS
Candidiasis, oral (thrush) *(continued)*			
AIDS patient			
Stomatitis, esophagitis, vaginitis Oral colonization with candida correlates with HIV RNA levels in plasma less so with CD4 counts *(JID 180 534 1999)* Protease inhibitors appear to ↓ recurrent oral candidiasis themselves vs rx with other antiretroviral agents (p< 001) *(J AIDS 21 20 1999)* May be due to direct effect on candida aspartic protease *(J AIDS 22 106 1999)*	**Fluconazole** 200 mg po 1st day then 100 mg qd x14 d (21 d or 2 wks following resolution of symptoms for esophagitis) or **Itraconazole** oral solution 200 mg po qd or 100 mg po bid x14 d Some recommend oral topical agents[1] for oral without esophageal involvement when CD4 >50 & receiving (or will receive) HAART	**For fluconazole-refractory disease:** Options include 1 **Fluconazole** 400–800 mg po qd or bid or 2 **Itraconazole** solution 100 mg po bid or 3 **Ampho B** 0 3–0 5 mg/kg IV qd or 4 **Voriconazole** *(see Table 11B page 83 for dose)* or 5 **Ceapofungin** 50 mg IV qd	**Fluconazole-refractory disease remains low** (4% in ACTG 816) & is seen in pts with low CD4 counts (< 50/ mm³) **Flu** superior to oral suspension of **nystatin** *(CID 24 1204 1997)* **Itra** 100 mg po bid x14 d achieved clinical response in 41/74 (55%) pts unresponsive to flu *(AIDS Res Hum Retrovir 15 1413, 1999)* **Ampho B oral suapension** gave 42 6% response rate in 54 pts refractory to **flu** but 70% of those relapsed *(AIDS 14 845 2000)* For esophagitis **caspofungin** as effective as **empho B IV** but less toxic *(CID 33 1529 2001 AAC 46 451 2002 J AIDS 31 183 2002)* **Voriconazole anidulafungin & micafungin** as effective as **fluconazole** for esophagitis *(CID 33 1447, 2001, CID 39 770 & 842 2004)*
Post-treatment chronic suppresaion (secondary prophylaxis) for disabling recurrent oral esophageal infection Authors would dc if sustained CD4 count ↑ (>200/ mm³) following HAART	**Current recommendation is to avoid chronic suppressiva rx** & only rx acute episode *(AIDS Res Hum Retroviruses 10 1619 1999)* However some use **fluconazole** 100 mg po qd to 100–150 mg po q week	If fluconazole-refractory esophagitis i e failed flu suppression may be forced to rx with **ampho B** (0 3 mg/kg IV qd or 1 mg/kg IV q week)	Fluconazole 200 mg qd does reduce risk of candida esophagitis & cryptococcosis *(NEJM 332 700 1995)* Disadvantages Concern of enhanced risk of emergence of fluconazole (azole)-resistant Candida species
Peritonitis (Chronic Ambulatory Peritoneal Dialysis) *See Table 19 page 137*	**Fluconazole** 400 mg po qd x2–3 wks	**Ampho B** continuous IP dosing at 1 5 mg/L of dialysis fluid x4–6 weeks	Remove cath immediately or if no clinical improvement in 4–7 d
Urinary: Candiduria • Usually colonization of urinary catheter a benign event • Rarely may be source of dissemination if pt has obstructive uropathy or marker of acute hematogenous dissemination Persistent candiduria in immunocompromised pt warrants ultrasound or CT of kidneys	**Remove urinary cathetar or stant** 40% will clear but only 20% if replaced *(CID 30 14 2000)* Antifungal rx not indicated unless pt has symptoms of UTI, neutropenic, low birth-weight infant has renal allograft or is undergoing urologic manipulation Then **fluconazole** 200 mg/d po or IV x7-14 d OR **ampho B** 0 5 mg/kg/d IV x7 14 d		**Fluconazola** alone is successful in presence of bezoar *(Ped Nephrol 17 550, 2002)* In a placebo controlled trial candiduria was cleared more rapidly in pts treated with flucon 200 mg/d x14 d but 2 weeks after completion was not different than placebo group 60% for catheterized pts & 73% for non-catheterized pts *(CID 30 15 2000)* **Bladder washout** with ampho B not recommended will not treat upper tract infection 5FC may be of value in non albicans UTI but resistance develops rapidly **Caspofungin** was effective in clearing candiduria in 12 pts (most with candidemia) but urine levels low *(IDSA 2003 Abst 135)* **NOTE:** Vori not in urine in active form
Vaginitis—Non-AIDS patients *Review article MMWR 51(RR-6) 2002* (Candida vaginitis in AIDS patients *see Stomatitis vaginitis above)* *(See Table 1 page 17)*			
Sporadic/infrequent	**Oral Fluconazole** 150 mg po x1 **OR itraconazole** 200 mg po bid x1 d	**Intravaginal:** Multiple **imidazoles** with 85–95% cure rates See doses in footnote[2] ** for over-the-counter preparations see below in footnote[1]	**In ganeral, oral & vaginal rx are aimilerly affective.** Rx aided by avoiding tight clothing e g pantyhose Oral drugs ↓ rectal candida & may ↓ relapses Fluconazole resistance in both HIV+ & HIV neg pts *(CID 22 726 1996)* Incidence of flu-refractory disease remains low *(CID 26 557 1998)* Boric acid solution intravaginally has also been used *(CID 24 649 1997)*
Chronic recurrent (5–8%) ≥4 episodes/yr Ref *NEJM 351 876 2004*	**Fluconazole** 150 mg po qd x3 & then 150 mg po q wk		After 6 mos >90% of 170 women free of disease vs 36% of 173 receiving placebo maintenance By 6 mos off rx 42 9% free of disease vs 21 9% who received placebo (p <0 001)

[1] **Oral aganta:** Nystatin clotrimazole troche 10 mg 5x/d

[2] **Butaconazola** 2% cream (5 gm) qd hs x3 d** or 2% cream SR 5 gm x1 or **clotrimazole** 100 mg vaginal tabs (2 qd hs x3 d) or 1% cream (5 gm) qd hs x7 d (14 d may ↑ cure rate) or 100 mg vaginal tab x7 d or 500 mg vaginal tab x1 or **miconazole** 200 mg vaginal suppos (1 qd hs x3 d**) or 100 mg vaginal suppos qd x7 d or 2% cream (5 gm) qd hs x7 d or **terconazole** 80 mg vaginal tab (1 qd hs x3 d) or 0 4% cream (5 gm) qd hs x7 d or 0 8% cream 5 gm intravaginal qd x3 d or **tioconazole** 6 5% vag ointment x1 dose** ** – over the counter product

* From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is avaraga wholasale price (AWP).**

See page 81 for abbreviations All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (5)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
"Candida syndroma"	In a double-blind study **nyatatin did not reduce ayatemic or psychological aymptoma** vs placebo *(NEJM 323 1717 1990)*		
Chromomycosis *(J Am Acad Derm 44 585 2001)* (Cladosporium or Fonsecaea) Cutaneous (usually feet legs)	If lesions small and few **surgical excision or cryosurgery with liquid nitrogen** *(Int J Dermatol 42 408 2003)* If lesions chronic extensive burrowing **itraconazole**	**Itraconazole** 100 mg po qd x18 months (or until response) [NFDA1] Fluconazole experience disappointing	**13/13 patients rx itra responded** 2 relapses (18 24 mos) *(CID 15 553 1992)* Terbinafine[FDA] impressive in a small number of pts *(Expert Opin Pharm Ther 5 247 2004)* In 4 pts resistance to itra developed on rx with 2 clinical failures *(Mycosis 47 216 2004)*
Coccidioidomycosis (Coccidioides immitis) *(see AnIM 130 293 1999 IDCP 8 21 1999 CID 30 658 2000, ID Clin N A 17 41 2003 Med 83 149 2004)*			
Primary pulmonary (San Joaquin or Valley Fever) Pts low risk persistence/complication	**Antifungal rx not generally recommended** but pt should be monitored periodically and rx if fever wt loss and/or fatigue do not resolve within several wks to 2 months *(see below)*		Uncomplicated pulmonary in normal host Influenza like illness of 1 2 wks duration.
Primary pulmonary in pts with ↑ risk for complications or dissemination. Rx indicated: • Immunosuppressive disease (AIDS) post transplantation or therapies (steroids TNF α antagonists) *(Arth Rheum 50 1959, 2004)* • Pregnancy in 3rd trimester • Diabetes • CF antibody >1 16 • ↑ pulmonary infiltrates • Dissemination (identification of spherules or culture of organism from ulcer, joint effusion pus from abscess or bone bx etc)	**Mild to moderate severity:** **Itraconazole** solution 200 mg po or IV bid OR **Fluconazole** 400 mg po qd for 3–12 months **Locally severe or disseminated disease:** **Ampho B** 0 6–1 mg/kg/d x7 d then 0 8 mg/kg/qod Total dose 2 5 gm or more followed by **itra** or **flu** **Consultation with specialist recommended:** surgery may be required		**Ampho B cure rate 50–70%. Responses to azoles are similar** Itra may have slight advantage esp in soft tissue infection Relapse rates after rx 40% Relapse rate ↑ if ↑ CF titer ≥1 256 (RR= 4 7) or neg coccidioidin skin test (RR=4 8) *(CID 25 1205 1997)* Following CF titers after completion of rx important rising titers warrant re-administration of rx *(CID 25 1211 1997)* In an RDBS[2] of 198 pts with progressive non-meningeal cocci 57% responded to flu vs 72% to itra (p=0 05) *(AnIM 133 676 2000)* Those with skeletal infections responded twice as frequently to itra than flu Relapse after dc rx 28% after flu 18% after itra Lifetime suppression in HIV+ patients flu 200 mg po qd or itra 200 mg po bid *(Mycosis 46 42 2003)* Targeted fluconazole prophylaxis for pt with hx of cocci or sero-pos may reduce reactivation post-transplant *(Transpl Inf Dis 5 3 2003)* Caspofungin successful in a renal transplant pt *(CID 39 879 2004)*
Meningitis occurs in 1/3 to 1/2 of pts with disseminated coccidioidomycosis			
Adult	**Fluconazole** 400–800 mg qd po indefinitely	**Ampho B** IV as for pulmonary *(above)* + 0 1–0 3 mg daily intrathecal (intraventricular) via reservoir device **OR itra** 400–800 mg qd **OR voriconazole** *(see Comment)* **OR caspo** *(see Comment)*	**80% relapse rate, continue flucon indefinitely** *(AnIM 124 305 1996)* Voriconazole successful in high doses (6 mg/kg q12h IV) followed by oral suppression (400 mg q12h po) *(CID 36 1619 2003)* & in a pt who failed flu liposomal ampho B + intrathecal ampho B *(AAC 48 2341, 2004)* Caspofungin also used *(JAC 54 292 2004)*
Child	**Fluconazole** (po) (Pediatric dose not established 6 mg/kg qd used)		
Cryptococcosis *(CID 30 710 2000)*			
Non-meningeal (non-AIDS) Risk 57% in organ transplant *(Transpl Inf Dis 4 183, 2002)*	**Fluconazole** 400 mg/d IV or po for 8 wks to 6 mos **For more severe disease:** **Ampho B** 0 5–0 8 mg/kg/d IV till response then change to **fluconazole** 400 mg qd po for 8–10 week course	**Itraconazole** 200-400 mg solution qd for 6 12 mos OR **Ampho B** 0 3 mg/kg/d IV + **flucytosine** 37 5 mg/kg[1] qid po x6 wks	Adjust flucyt dose & interval to produce serum levels of peak 70–80 mg/L trough 30–40 mg/L **Flucon alone 90% effective for meningeal and non-meningeal forms** (74% on steroid rx) Studies suggest fluconazole as effective as ampho B *(CID 22 S154 1996, CID 32 E145 2001)* Addition of interferon-γ (INF-γ-1b 50 μg/M² SC 3x/wk x9 wks) to liposomal ampho B assoc with response in pt failing antifungal rx *(CID 38 910, 2004)*
Meningitis (non-AIDS)	**Ampho B** 0 5–0 8 mg/kg/d IV + **flucytosine** 37 5 mg/kg[1] q6h po until pt afebrile and cultures negative (~6 weeks) *(NEJM 301 126 1979)* then stop ampho B/flucyt start **fluconazole** 200 mg po qd *(AnIM 113 183, 1990)* OR **Fluconazole** 400 mg qd po x8–10 weeks (less severely ill patient) Some recommend flu for 2 yrs to reduce relapse rate (no controlled data available) *(CID 28 297 1999)*		**Flucytosine levels must be measured;** adjust dose and interval to give serum levels peak 70–80 mg/L trough 30–40 mg/L **Fluconazole alone used successfully** comparative clinical trials lacking *(NEJM 330 263 1994)* Hydrocephalus may be successfully rx with VP[2] or VA[2] shunting *(CID 28 629 1999)* poor response if pts in coma *(CID 37 673 2003)*

[1] Some experts would reduce to 25 mg/kg q6h
[2] **VP** = ventriculoperitoneal **VA** = ventriculoatrial **RDBS** = randomized double-blind study
• From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is average wholesale price (AWP).**

See page 81 for abbreviations *All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 11A (6)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE — PRIMARY	ANTIMICROBIAL AGENTS OF CHOICE — ALTERNATIVE	COMMENTS
Cryptococcosis *(continued)*			
HIV+/AIDS: Cryptococcemia and/or Meningitis			
Treatment *(see CID 30 710, 2000)* ↓ in era of HAART *(Neurol 56 257, 2001, CID 36 789, 2003)* but still common when pt presents with AIDS & HIV status unknown *(AIDS 18 555, 2004)* Cryptococci in blood may be manitest by positive blood culture or positive test of serum for cryptococcal antigen With HAART symptoms of acute meningitis may return immune reconstitution *(AIDS 12 1491 1999)* If failure to respond to initial rx think dual infection with tbc neurosyphilis toxo etc *(Neurol 51 1213, 1998)*	**Ampho B 0.7–1 mg/kg/d. IV + flucytosine[1] 25 mg/kg po q6h x2 wks** or until clinically stable **followed by flu 400 mg/d. for minimum of 10 wks** then switch to 200 mg qd (suppression) *(see below)* or **Ampho B** alone 0.7–1.0 mg/kg/d IV x2 wks or until afebrile headache nausea and vomiting gone Then dc ampho B start **flucon** 400 mg po qd to complete 8–10 week course Then maintain on flucon 200 mg po qd Start Highly Active Antiretroviral Therapy (HAART) if possible	**Fluconazole** 400 mg po qd x6–10 wks then suppressive rx *(see Comments)* or **Fluconazole** 400 mg po qd + flucytosine 37.5 mg/kg po q6h x10 wks (↑ toxicity) or **Liposomal amphotericin** 5 mg/kg/d x2 wks followed by fluconazole as above *(Mycosis 46 24 2003)* or **Ampho B lipid complex** IV 5 mg/kg/d x2 wks then 3x/wk x4 wks[NFDA-I] *(CID 22 315 1996)*—poor results with <3 mg/kg	If normal mental status >20 cells/mm³ CSF and CSF crypto antigen <1 1024 flucon alone is reasonable *(CID 22 322, 1996)* Serum cryptococcal antigen useful in dx (95% sens) If ↑ CSF pressure, lower with CSF removal Must monitor 5-FC levels peak 70–80 mg/L trough 30–40 mg/L Higher levels assoc with bone marrow toxicity Itraconazole does not penetrate CSF *(CID 22 329, 1996)* In 64 pts ampho + 5FC ↓ crypto CFU³ in CSF more rapidly than ampho + fluconazole or combination of all 3 drugs (p <0.001) *(Ln 363 1764, 2004)* Even with rx (ampho B + 5FC regimen) 29/236 pts died within 1st 2 wks & 62 (26%) by 10 wks only 129 (55%) were alive & culture-neg at 10 wks *(CID 28 82 1999)* Also addition of INF-γ lb 100 µg SC tiw x10 wks ↑ rate of sterilization of CSF at 2 wks (36%) vs antifungal rx (ampho B + 5FC) alone (13%) *(JID 189 2185 2004)* In 163 pts (15 on HAART) survival was 85% 6 months after discharge from hospital & receiving flucon suppression in Uganda *(IDSA 2003, Abst 630)*
Suppression	**Fluconazole** 200 mg/d po [If CD4 count rises to >100/mm³ with effective antiretroviral rx most authorities now recommend dc suppressive rx See www.hivatis.org]	**Ampho B** 1.0 mg/kg IV 1x/week or **Itraconazole** 200 mg po bid if flu intolerant or failure	Itraconazole not as effective as fluconazole Not recommended No recurrences of crypto meningitis in 22 pts who dc flu suppression with >100 CD4 & undetectable VL x3 mos in Thailand *(CID 36 1329, 2003)* Only 4/100 with >100 CD4 relapsed with 2-year follow-up return of+ serum CRAG might predict relapse *(CID 38 565,2004)*
Dermatophytosis			
Erythrasma (Corynebacterium minutissimum)	**Erythromycin** 250 mg qid po x14 d	2% aqueous clindamycin topically	Diff dx with Tinea versicolor Tinea cruris Erythrasma gives coral red fluorescence with Woods light
Onychomycosis (Tinea unguium) *(Brit J Derm 148 402, 2003 Am J Clin Derm 5 225 2004 Cutis 74 516 2004)* A topical nail lacquer (ciclopirox) approved but cure in only 5–9% after 48 wks *(Med Lett 42 51 2000)* but ↑ to 50% cure in another study *(J Am Acad Derm 44 479 2001, Cutis 73 81, 2004)* May enhance oral rx *(Cutis 74 55, 2004)* Terbinafine ↑ cure rate & ↓ relapse vs itra at 5 yrs *(ArDerm 138 353 2002)* & ↑ cure rate after 1 yr vs flu *(Brit J Derm 142 97 2000)* appears to be most cost-effective rx *(Manag Care 12 47, 2003)*	**Fingernail Rx Options:** **Terbinafine**[2] 250 mg po qd [children <20 kg 67.5 mg/d 20–40 kg 125 mg/d >40 kg 250 mg/d] x6 wks (79% effective) or **Itraconazole**[3] 200 mg po qd x3 mos [NFDA-I] or **Itraconazole** 200 mg po bid x1 wk/mo x2 mos or **Fluconazole** 150–300 mg po q wk x3–6 mos [NFDA-I] **NOTE:** *For side-effects see footnotes* **2** & **3**	**Toenail Rx Options:** **Terbinafine**[2] 250 mg po qd [children <20 kg 67.5 mg/d 20–40 kg 125 mg/d >40 kg 250 mg/d] x12 wks (76% effective) or **Itraconazole**[3] 200 mg po qd x3 mos (59% effective) or **Itraconazole** 200 mg bid x1 wk/mo x3–4 mos (63% effective)[NFDA-I] or **Fluconazole** 150–300 mg po q wk x6–12 mos (48% effective)[NFDA-I] [Data reflect cure rate from meta-analysis of all randomized controlled trials *(Brit J Derm 150 537 2004)*]

[1] Flucytosine = 5-FC

[2] **Serious but rare cases of hepatic failure** have been reported in pts receiving terbinafine & should not be used in those with chronic or active liver disease *(See Table 11B page 83)* Suggest checking ALT & AST before prescribing *(Am J Health Sys Pharm 58 1076 2001)*

[3] Use of itraconazole has been associated with myocardial dysfunction and with onset of congestive heart failure *(see Ln 357 1766 2001)*

* From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is average wholesale price (AWP).**

See page 81 for abbreviations All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE: PRIMARY	ANTIMICROBIAL AGENTS OF CHOICE: ALTERNATIVE	COMMENTS
Dermatophytosis *(continued)* **Tinea capitis ("ringworm")** (Trichophyton tonsurans Microsporum canis N America other sp elsewhere) *(PIDJ 18 191 1999)*	**Terbinafine** *(see footnote 2 page 78)* 250 mg po qd x4 wks for T tonsurans 4–8 wks for Microsporum canis[NFDA-I] Children 125 mg (or 6–12 mg/kg/d) po qd *(COID 17 97, 2004 Expert Opin Pharm Ther 5 219 2004 J Eur Acad Dermatol Venereol 18 155 2004)*	**Itraconazole** *(see footnote 3 page 78)* 3–5 mg/kg/d for 30 d [NFDA-I] **Fluconazole** 8 mg/kg qwk x8-12 wks [NFDA-I] Cap at 150 mg po q wk for adults **Griseofulvin** adults 500 mg po qd x4–6 wks children 10–20 mg/kg/d until hair regrows, usually 6–8 wks	All agents with similar cure rates (60-100%) in clinical studies *(Ped Derm 17 304 2000)* Griseofulvin considered drug of choice by some although concerns for resistance and toxicities Addition of topical ketoconazole or selenium sulfate shampoo reduces transmissibility *(J J Derm 39 261 2000)*
Tinea corporis, cruris, or pedis (Trichophyton rubrum T mentagrophytes, Epidermophyton floccosum) 'Athlete s foot jock itch " and ringworm	**Topical rx:** Generally applied 2x/d Available as creams ointments sprays by prescription & over the counter Apply 2x/d for 2–3 wks See footnote[1] for names and prices Recommend Lotrimin Ultra or Lamisil AT contain butenafine & terbinafine—both are fungicidal	**Terbinafine** 250 mg po qd x2 wks[NFDA-I] OR **ketoconazole** 200 mg po qd x4 wks OR **fluconazole** 150 mg po 1x/wk for 2–4 wks[NFDA-I] **Griseofulvin** adults 500 mg po qd x4–6 wks children 10–20 mg/kg/d Duration 2-4 wks for corporis 4-8 wks for pedis	Keto po often effective in severe recalcitrant infection Follow for hepatotoxicity Terbinafine 87% achieved mycological cure in double-blind study (32 pts) *(J Med Assn Thai 76 388 1993 Brit J Derm 130(S43) 22 1994)* and fluconazole 78% *(J Am Acad Derm 40 S31 1999)*
Tinea versicolor (Malassezia furfur or Pityrosporum orbiculare)	**Ketoconazole** (400 mg po single dose)[NFDA-I] or (200 mg qd x7 days) or (2% cream applied 1x qd x2 wks)	**Fluconazole** 400 mg po single dose or **Itraconazole** 400 mg po qd x3–7 days	Keto (po) x1 97% effective in 1 study Another alternative Selenium sulfide (Selsun) 2 5% lotion apply as lather leave on 10 min then wash off 1x/d x7d or 3–5x/week x2–4 weeks
Fusariosis Infections in eye skin sinus & disseminated diseases—↑ in transplant pts *(CID 34 909 2002, Clin Micro Inf 10 567, 2004))*	**Voriconazole** 6 mg/kg IV q12h on day 1 then either (4 mg/kg q12h) or (200 mg po q12h for body weight ≥40 kg but 100 mg po q12h for body weight <40 kg)	**Ampho B** 1–1 2 mg/kg or **lipid-associated ampho B**	Voriconazole successful in 9/21 4 eye, 2 bloodstream 2 sinus & 1 skin *(CID 35 909, 2002, 36 1122 2003 37 311, 2003)*
Histoplasmosis (Histoplasma capsulatum) *See CID 30 688 2000 ID Clin N A 17 1 2003* Best diagnostic test is urinary antigen (ELISA) *(CID 22 S102, 1996)* MiraVista Diagnostics (1-866-647-2847) **Immunocompetent patient:** Pulmonary localized disseminated	**Minimal disease: No rx** **Moderate: Itraconazole** 200 mg/d solution po for 9 months If life-threatening 200 mg po tid x3 d then 200 mg po bid until response [2] If IV rx necessary Dose 200 mg IV bid x4 doses followed by 200 mg IV qd *(see Table 10B)* **Severe, including meningitis: Ampho B** 0 5–1 mg/kg/d IV x7 d followed by 0 8 mg/kg qod IV **Itra not recommended for meningitis** *(South Med J 96 410, 2003)* *(See CID 38 463 2004)*		**With ≥2 months itra rx, 86% success in chronic pulmonary & extrapulmonary** *(AJM 93 489, 1992)* Antifungal rx not useful for histo fibrous mediastinitis Clinical Severe—Temp >39 5°C Karnofsky <60, albumin <3 gm/dl hepatic enzymes >5x normal WBC <500 platelets <50 000 creatinine >6 mg/dl *[CID 19(Suppl 1) S19 1994]* **Flu less effective then itra** *(CID 23 996 1996)*
Immunocompromised patient (AIDS) *(CID 24 1195, 1997, & 32 1215 2001)* Recently reported following antitumor necrosis factor-α rx infliximab *(AJRCCM 167 1279 2003)* Risk factors for death dyspnea platelet count <100 000/mm³ & LDH >2x upper limit normal *(CID 38 134, 2004)*	**For moderate to severe disease: Lipid-based Ampho B: Liposomal Ampho B** 3 mg/kg/d IV x14 d then suppressive therapy with **itraconazole** 200 mg po qd *(AnIM 137 435 2002)* OR **Ampho B** 0 5–1 mg/kg/d IV x7 d followed by 0 8 mg/kg qod (or 3x/week) to total dose of 10–15 mg/kg then suppressive therapy as above	**For less severe disease: Itraconazole** (300 mg bid po x3 d then 200 mg bid po x12 wks) or (400 mg qd x12 wks (85–90% response) then 200 mg qd *(see footnote 3 page 78)* **Not recommended for meningitis.** IV if unable to take po	Liposomal Ampho B superior at 2 weeks vs Ampho B (88% vs 64% clinical success) in 81 patients with a decrease in nephrotoxicity (97% vs 37%) No difference in mortality after 10 additional weeks of itra in both arms *(AnIM 137 105 2002)* **Itra (ACTG 120) 50/59 (85%) pts responded,** cleared fungemia with only 5% toxicity 1 pt with meningitis failed 2 failed because of low serum levels Avoid rifampin reduces itra serum concentration *(AJM 98 336 1995)* **Itra beat drug for suppression at 200 mg qd** but 3/46 had probable hepatic toxicity *(J AIDS & Human Retro 16 100, 1997)* Flu less effective than itra & induces flu resistance *(CID 33 1910, 2001)* Suppression can be safely dc after 12 mos of antifungal rx & 6 mos of HAART if CD4 count >150 0 relapses after 2-yr follow-up in 32 pts *(CID 38 1485 2004)*
Madura foot *(See Comments)(See Nocardia, Pseudallescheria boydii, below)*	None, unless Nocardia *(see below)*	In U S usually Pseudallescheria boydii (Petrolidium spp) Miconazole IV agent of choice [NUS] In Mexico usually Nocardia brasiliensis, in Japan, N asteroides	

[1] Drug name (trade name) & wholesale price for 15 gm All are applied to affected area bid **Prescription drugs:** butenafine (Mentax) $27 ciclopirox (Loprox) $12 clotrimazole (Lotrimin $13, Mycelex $10) econazole (Spectazole) $13 ketoconazole (Nizoral) $15 miconazole (Micatin, Monistat-Derm) NB $5–13 G $3 naftifine (Naftin) $17 oxiconazole (Oxistat) $14 sulconazole (Exelderm) $10, terconazole (Terazol) $9, sertaconazole (Ertaczo) $45 24 **Non-prescription (over-the-counter):** Tolnaftate (Tinactin $5 Ting or Tolnate $2), undecylenic acid (Cruex $5 Desenex $5) Lotrimin 1% 12 gm $6 17 Lamisil AT 1% 12 gm $6 79

[2] **Oral solution preferred to tablets because of ↑ absorption** *(see Table 11B, page 83)*

* From 2004 Drug Topics Red Book, Medical Economics Data and Hospital Formulary Pricing Guide **Price is average wholesale price (AWP).**

See page 81 for abbreviations All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (8)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Mucormycosis (Zygomycosis—Rhizopus Rhizomucor Absidia) Rhinocerebral pulmonary *(ArIM 159 1301, 1999)*	**Ampho B** Increase rapidly to 0 8–1 5 mg/kg/d IV when improving then qod Total dose usually 2 5–3 gm or **Lipid-baaed Ampho B. Azoles and caepofungin usually inactive**		Treatment requires control of underlying condition esp diabetic ketoacidosis neutropenia Surgical debridement usually required and discontinue deferoxamine if applicable Deferoxamine ↑ risk of mucormycosis, use hydroxpyndinone chelators deferiprone *(Phase 3 study* Apotex *847-573-9999)* High-dose (10–15 mg/kg/d) liposomal amphotericin successful in 2 cases *(J Inf 41 265 2000)* 1 pt who failed ampho B responded to posaconazole a new triazole under development *(CID 36 1488 2003)*
Nocardiosis (N asteroides & N brasiliensis) Culture & sensitivities may be valuable in refractory cases Reference Labs R J Wallace (903) 877-7680 or CDC (404) 639-3158 *(IDCP 8 27, 1999)*			
Cutaneous and lymphocutaneous (sporotrichoid)	**TMP/SMX** 5–10 mg/kg/d of TMP & 25–50 mg/kg/d of SMX in 2–4 div doses/d po or IV	**Sulfisoxazole** 2 gm po qid or **minocycline** 100–200 mg po bid	Linezolid 300–600 mg po bid x3–24 mos successful in 6/6 pts 4 with disseminated disease of whom 2 had brain abscesses *(CID 36 313, 2003)* Found to be very active in vitro & in vivo *(AAC 48 832 2004)*
Pulmonary, disseminatad, brain abacess Duration of rx generally 3 mos for immunocompetent host (38%) & 6 mos for immunocompromised (62% organ transplant malignancy chronic lung disease diabetes ETOH use steroid rx & AIDS)	**TMP/SMX** Initially 15 mg/kg/d of TMP & 75 mg/kg/d of SMX IV or po div in 2–4 doses After 3–4 wks ↓ dose to 10 mg/kg/d TMP in 2–4 doses po Do serum level *(see Comment)*	(**IMP** 500 mg IV q6h) + (**amikacin** 7 5 mg/kg IV q12h) x3–4 wks & then po regimen	Survival may be improved when sulfa-containing regimen used *(Medicine 68 38 1999)* Prosthetic valve endocarditis with N asteroides cured with IMP + amikacin x2 mos followed by TMP/SMX x4 mos *(Am J Med 115 330 2003)* Measure sulfonamide blood levels early to ensure absorption of po rx Desire peak level of 100–150 µg/ml 2 hrs post-po dose
Paracoccidioidomycosis (South American blastomycosis)/P brasiliensis	**Itraconazole** 200 mg/d po x 6 months or **Ketoconazole** 400 mg/d po for 6–18 months	**Ampho B** 0 4–0 5 mg/kg/d IV to total dose of 1 5–2 5 gm or **sulfonamides** *(dose see Comment)*	Improvement in >90% pts on itra or keto [NFDA†] Sulfa 4–6 gm/d for several weeks then 500 mg/d for 3–5 yrs also used *(CID 14 (Suppl) S-68, 1992)* Low-dose itra (50–100 mg/d) keto (200–400 mg/d) & sulfadiazine (up to 6 mg/d) showed similar clinical responses in 4–6 mos in a randomized study 14/14 14/14 13/14 respectively *(Med Mycol 40 411, 2002)* HIV+ TMP/SMX suppressive rx indefinitely *(CID 21 1275, 1995)* Terbinafine has good in vitro activity *(JCM 40 2828 2002)*
Lobomycosis (keloidal blastomycosis)/ P loboi	**Surgical excision clofazimine** or **empho B**		
Penicilliosis (Penicillium marneffei) Common disseminated fungal infection in AIDS pts in SE Asia (esp Thailand & Vietnam) *(CID 24 1080, 1997 Intl J Inf Dis 3 48 1998)*	**Ampho B** 0 5–1 mg/kg/d x2 wks followed by **itraconazole** 400 mg/d for 10 wks followed by 200 mg/d po **Indefinitely for HIV-Intected pts** *(CID 26 1107 1998)* *See Comment*	**Itra** 200 mg po tid x3 d then 200 mg bid po x12 wks then 200 mg po qd [1] (IV if unable to take po)	3rd most common OI in AIDS pts in SE Asia following TBc and cryptococcal meningitis May resemble histoplasmosis or TBc *(CID 23 125 1996)* Skin nodules are umbilicated (mimic cryptococcal infection or molluscum contagiosum) In AIDS pts long-term suppression with itra was effective in **prevanting relapaas in 36/36 pts** whereas 20/35 pts receiving placebo relapsed within 6 mos *(NEJM 339 1739, 1998)*
Phaeohyphomycosis (black molds/ dematiaceous fungi) *(See CID 34 467 2002)* Sinuses skin brain abscess **Species Scadosporium prolificana** Bipolaris Wangiella Curvularia Exophiala Phialemonium Scytalidium Alternaria & others)	**Surgary** + **itraconazole** 400 mg/d po duration not defined probably 6 months[NFDA†]	**Voriconazole** has some in vitro activity but clinical experience limited to date vs S prolificans *(AAC 45 2151 2001)* **Itraconazole** + **terbinafine** synergistic against S prolificans *(AAC 44 470 2000)* No clinical data but combination could show ↑ toxicity *(see Table 11B page 83)*	Notoriously resistant to antifungal rx including amphotericin & azoles *(CID 34 909 2002)* Mortality >80% Cause of disseminated disease in immunosuppressed pts (3/4) esp neutropenia [accounted for 10% of mycelial infections post-transplant *(CID 37 221 2003)*] & fungal endocarditis esp porcine valve Blood cultures pos in >50% eosinophilia in 11%
Scadosporium aprospermum (Pseudallescheria boydii) (not considered a true dematiaceous mold) *(Med 81 333 2002)* Skin subcutaneous (Madura foot) brain abscess recurrent meningitis	**Voriconazole** 6 mg/kg IV q12h on day 1 then either (4 mg/kg IV q12h) or (200 mg po q12h for body weight ≥40 kg, but 100 mg po q12h for body weight < 40 kg) *(PIDJ 21 240, 2002)*	Surgery + **itraconazole** 200 mg po bid until clinically well [NFDA†] (Many species now resistant or refractory to itra) or **Miconazole**[1] – 600 mg IV q8h	Notoriously resistant to antifungal drugs including amphotericin In vitro voriconazole more active than itra *(J Clin Micro 39 954, 2001)* Case reports of successful rx of disseminated and CNS disease with voriconazole *(CID 31 1499 & 673, 2000 Clin Microbiol Inf 9 750 2003, EJCMID 22 408 2003)*

[1] **Oral solution pretarrad to tablets bacause of ↑ abaorption** *(see Table 11B page 83)*

* From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is averaga wholasala price (AWP)**

See page 81 for abbreviations All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11A (9)

TYPE OF INFECTION/ORGANISM/ SITE OF INFECTION	ANTIMICROBIAL AGENTS OF CHOICE		COMMENTS
	PRIMARY	ALTERNATIVE	
Sporotrichosis *(CID 29 231 1999 CID 30 684 2000 CID 36 34 2003 ID Clin N A 17 59 2003)*			
Cutaneous/Lymphonodular	**Itraconazole** 100–200 mg/d solution po x3–6 mos (then 200 mg po bid long-term[1] for HIV-infected pts[NFDA-I])	**Fluconazole** 400 mg po qd x6 mos or Sat soln potassium iodide (**SSKI**) (1 gm of KI in 1 ml of H_2O) Start with 5–10 drops tid gradually ↑ to 40–50 drops tid for 3–6 mos Take after meals	Itra ref *CID 17 210 1993* Some authorities use ampho B as primary therapy Ampho B resistant strains reported *(AJM 95 279 1993)* Itra rx for up to 24 months effective in multifocal osteoarticular infection *(CID 23 394 1996)* SSKI side effects nausea rash fever metallic taste salivary gland swelling
Extracutaneous Osteoarticular pulmonary disseminated meningeal	**Osteoarticular, pulmonary: Itraconazole** 300 mg po bid x6–12 mos then 200 mg po bid (long-term for HIV-infected pts) (IV if unable to take po)	**Disseminated, meningeal: Ampho B** 0.5 mg/kg/d to total of 1–2 gm followed by **itra** 200 mg bid or **flu** 800 mg qd	

Abbreviations: **AM/CL** = amoxicillin clavulanate **Ampho B** = amphotericin B **Clot** = clotrimazole **dc** = discontinue **Flu** = fluconazole **Flucyt** = flucytosine **G** = generic **Griseo** = griseofulvin **I** = investigational **IMP** = imipenem **IT** = intrathecal or intraventricular **Itra** = itraconazole **IUD** = intrauterine contraceptive device **Keto** = ketoconazole **NB** = name brand **NFDA-I** = not FDA-approved indication **NUS** = not available in the U.S. **PSL** = peak serum level **R/O** = rule out **TMP/SMX** = trimethoprim/sulfamethoxazole **vag. oint.** = vaginal ointment

TABLE 11B: ANTIFUNGAL DRUGS: ADVERSE EFFECTS, COMMENTS, COST

DRUG NAME, GENERIC (TRADE)/ USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
Non-lipid amphotericin B deoxycholate (Fungizone) 0.3–1 mg/kg/d as single infusion 50 mg $28 Mixing ampho B with lipid emulsion results in precipitation and is discouraged *(Am J Hlth Pharm 52 1463, 1995)*	**Admin.:** Ampho B is a colloidal suspension that must be prepared in electrolyte-free D5W at 0.1 mg/ml to avoid precipitation. No need to protect drug suspensions from light. Ampho B infusions cause chills/fever, myalgia, anorexia, nausea, rarely hemodynamic collapse/hypotension. Postulated due to proinflammatory cytokines but does not appear to be histamine release *(Pharmacol 23 966 2003)* Manufacturer recommends a test dose of 1 mg, but often not done (1st few ml of 1st dose is a test dose). Duration of infusion usually 4 or more hrs. No difference found in 1 vs 4-hr infusions *(AAC 34 1402 1992)* except chills/fever occurred sooner with 1-hr infusion. Febrile reactions decrease with repeated doses. Rare pulmonary reactions (severe dyspnea and focal infiltrates suggesting pulmonary edema) associated with rapid infusion *(CID 33 75, 2001)* Severe rigors respond to meperidine (25–50 mg IV). Premedication with acetaminophen, diphenhydramine, hydrocortisone (25–50 mg) and heparin (1000 units) had no influence on rigors/fever *(CID 70 755 1995)* If cytokine postulate correct, NSAIDs or high-dose steroids may prove efficacious but their use may risk worsening infection under rx or increased risk of nephrotoxicity (i.e. NSAIDs). Clinical side effects ↓ with ↑ age *(CID 26 334 1998)* **Toxicity:** Major concern is nephrotoxicity (15% of 102 pts surveyed *CID 26 334 1998)* Manifest initially by kaliuresis and hypokalemia, then fall in serum bicarbonate (may proceed to renal tubular acidosis) ↓ in renal erythropoietin and anemia, and rising BUN/serum creatinine. Hypomagnesemia may occur Can reduce risk of renal injury by **(a) pre- and post-infusion hydration with 500 ml saline (if clinical status will allow salt load)** (b) avoidance of other nephrotoxins, e.g. radiocontrast, aminoglycosides, cis-platinum, (c) use of lipid prep of ampho B. Use of low dose dopamine did not significantly reduce renal toxicity *(AAC 42 3103, 1998)* In a single randomized controlled trial of 80 neutropenic pts with refractory fever & suspected or proven invasive fungal infection, 0.97 mg/kg/d amphotericin **continuously infused over a 24-hr period** was compared to the classical **rapid infusion** of 0.95 mg/kg/d **infused over 4 hrs**. Continuous infusion produced less nephrotoxicity [26% ↓ in max. serum Cr (p=0.005)], a reduction in fever, chills & vomiting (p <0.02–0.0003) & appeared as effective as rapid infusion but in very few proven fungal infections (7 & 3, respectively) *(BMJ 322 1 2001)* Continuous infusion also allows a dramatic ↑ in administered dosage without sig. toxicity *(CID 36 943 2003)* It is disturbing that these exciting observations have not led to controlled trials examining efficacy in rx of life-threatening fungal infections *(CID 36 952 2003)* Await trials of efficacy in larger number of proven fungal infections!
(continued on next page)	*(continued on next page)*

* From 2004 Drug Topics Red Book, Medical Economics Data and Hospital Formulary Pricing Guide. **Price is average wholesale price (AWP).**

See page 81 for abbreviations. All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11B-2

DRUG NAME, GENERIC (TRADE)/ USUAL DOSAGE/CDST*	ADVERSE EFFECTS/COMMENTS
(continued from previous page) **Lipid-based ampho B products:**[1]	*(continued from previous page)*
Amphotericin B lipid complex (ABLC) (Abelcet): 5 mg/kg/d as single infusion 100 mg IV $255 ($890/350 mg)	**Admin.:** Consists of ampho B complexed with 2 lipid bilayer ribbons Compared to standard ampho B larger volume of distribution rapid blood clearance and high tissue concentrations (liver spleen, lung) Dosage **5 mg/kg once daily** infuse at 2 5 mg/kg/hr adult and ped dose the same Do NOT use an in-line filter Do not dilute with saline or mix with other drugs or electrolytes [2] **Toxicity:** Fever and chills in 14–18% nausea 9% vomiting 8% serum creatinine ↑ in 11% renal failure 5% anemia 4% ↓ K 5%, rash 4%
Liposomal amphotericin B (L-AmB, AmBisome): 1–5 mg/kg/d as single infusion 50 mg $196 ($1372/350 mg)	**Admin.:** Consists of vesicular bilayer liposome with ampho B intercalated within the membrane Dosage **3–5 mg/kg/d** IV as single dose infused over a period of approx 120 min If infusion is well tolerated infusion time can be reduced to 60 min [2] 1 mg/kg/d was as effective as 4 mg/kg/d (6 mos survival rates 43% vs 37% respectively) in pts with invasive aspergillosis complicating bone marrow tx and/or neutropenia from malignancy *(CID 27 1406, 1998)* **Major toxicity:** Generally less than ampho B Nephrotoxicity 18 7% vs 33 7% for ampho B chills 47% vs 75% nausea 39 7% vs 38 7% vomiting 31 8% vs 43 9% rash 24% for both ↓ Ca 18 4% vs 20 9% ↓ K 20 4% vs 25 6% ↓ Mg 20 4% vs 25 6% Acute infusion-related reactions are common with liposomal ampho B 20–40% 86% occurred within 5 min of infusion including chest pain dyspnea & hypoxia or severe abdominal flank or leg pain 14% developed flushing & urticaria near the end of 4-hr infusion All responded to diphenhydramine (1 mg/kg) & interruption of L-AmB infusion These reactions may be due to complement activation by the liposome *CID 36 1213, 2003*
Amphotericin B cholesteryl complex (amphotericin B colloidal dispersion, ABCD, Amphotec): 3–4 mg/kg/d as single infusion 100 mg $160	**Admin.:** Consists of ampho B deoxycholate stabilized with cholesteryl sulfate resulting in a disc-shaped colloidal complex Compared to standard ampho B larger volume of distribution rapid blood clearance high tissue concentrations Dosage Initial dose for adults & children **3–4 mg/kg/day** If necessary can ↑ to 6 mg/kg/day Dilute in D5W & infuse at 1 mg/kg/hr Do NOT use in-line filter **Toxicity:** Chills 50% fever 33% ↑ serum creatinine 12–20% ↓ Ca 6%, ↓ K 17%
Caspofungin (Cancidas) 70 mg IV on day 1 followed by 50 mg IV qd (reduce to 35 mg IV qd with moderate hepatic insufficiency) 70 mg $515 50 mg $400 Ref *Ln 362 1142 2003*	An echinocandin which inhibits synthesis of β-(1 3)-D-glucan a critical component of fungal cell walls Fungicidal against candida (MIC <2 µg/ml) including those resistant to other antifungals & active against aspergillus (MIC 0 4–2 7 µg/ml) Serum levels on rec dosages = peak 12 trough 1 3 (24 hrs) µg/ml Approved for rx of candidemia & other candida infections (intra-abdominal abscess esophageal peritonitis pleural sponge infection) & refractory aspergillus infections & was 48 9% successful in 57 pts with invasive aspergillus infections in severely impaired hosts who had failed other antifungals **Toxicity** remarkably non toxic with no nephrotoxicity reported Only 2% of 263 pts in double-blind trial dc drug due to drug related adverse event *(Transpl Inf Dis 1 25 2002)* 14% had ↑ transaminases (similar to triazoles) Most common adverse effect pruritus at infusion site & headache fever, chills vomiting & diarrhea associated with infusion Drug metabolized in liver & dosage ↓ to 35 mg in moderate to severe hepatic failure Class C for pregnancy (embryotoxic in rats & rabbits) so only use if potential benefits outweigh risks *See Table 22, page 143 for drug-drug interactions, esp cyclosporine (hepatic toxicity) & tacrolimus (drug level monitoring recommended) (Curr Med Res Opin 19 263, 2003 JAC 49 889, 2002)*
Fluconazole (Diflucan)(available generically) 100 mg tabs $8 54 150 mg tabs $13 60 200 mg tabs $14 400 mg IV $135 Oral suspension 40 mg/ml $130/35 ml bottle	IV=oral dose because of excellent bioavailability **Pharmacology** absorbed po water solubility enables IV Peak serum levels *(see Table 9 page 60)* T½ 30 hrs (range 20–50 hrs) 12% protein bound **CSF levels 50–90% of serum in normals** ↑ in meningitis No effect on mammalian steroid metabolism **Drug-drug interactions common, see *Table 22*** Side-effects overall 16% [more common in HIV+ pts (21%)] Nausea 3 7% headache 1 9% skin rash 1 8% abdominal pain 1 7% vomiting 1 7% diarrhea 1 5% ↑ SGOT 20% Alopecia (scalp pubic crest) in 12–20% pts on ≥400 mg po qd after median of 3 months (reversible in approx 6 mos) *(AnIM 123 354 1995)* Rare severe hepatotoxicity, exfoliative dermatitis Anaphylaxis *(CID 13 81 1993)* thrombocytopenia leukopenia Good reference *NEJM 330 263, 1994*
Flucytosine (Ancobon) 500 mg cap $9	AEs Overall 30% GI 6% (diarrhea anorexia nausea vomiting) hematologic 22% [leukopenia thrombocytopenia when serum level > 100 µg/ml (esp in azotemic pts)] hepatotoxicity (asymptomatic ↑ SGOT reversible) skin rash 7% aplastic anemia (rare 2 or 3 cases) False ↑ in serum creatinine on EKTACHEM analyzer *JAC 26 171, 2000*
Griseofulvin (Fulvicin Grifulvin Grisactin) 500 mg G $1 56 susp 125 mg/ml 120 ml $36	Photosensitivity urticaria GI upset fatigue leukopenia (rare) Interferes with warfarin drugs Increases blood and urine porphyrins should not be used in patients with porphyria Minor disulfiram-like reactions Exacerbation of systemic lupus erythematosus

[1] Published data from patients intolerant of or refractory to conventional ampho B deoxycholate (Amp B d) **None of the lipid ampho B preps has shown superior efficacy compared to ampho B in prospective trials (except liposomal ampho B was more effective vs ampho B in rx of disseminated histoplasmosis at 2 wks** *(AnIM 137 105 2002 CID 37 415 2003)* **Dosage equivalency has not been established** *(CID 36 1500, 2003)* Nephrotoxicity ↓ with all lipid ampho B preps *(IDCP 7 516 1998 CID 27 603 1998 NEJM 340 764 1999)*

[2] Comparisons between Abelcet & AmBisome suggest higher infusion assoc toxicity (rigors) & febrile episodes with Abelcet (70% vs 36%) but a higher frequency of mild hepatic toxicity with AmBisome (59% vs 38% p=0 05) Mild elevations in serum creatinine were observed in 1/3 of both *(BJ Hemat 103 198 1998 Focus on Fungal Inf #9 1999 Bone Marrow Tx 20 39 1997, CID 26 1383 1998)*

* From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is average wholesale price (AWP).**

See page 81 for abbreviations All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

TABLE 11B (3)

DRUG NAME, GENERIC (TRADE)/ USUAL DOSAGE/COST*	ADVERSE EFFECTS/COMMENTS
imidazoles topical For vaginal and/or skin use	Not recommended in 1st trimester of pregnancy Local reactions 0 5-1 5% dyspareunia mild vaginal or vulvar erythema; burning pruritus urticaria resh Rarely similar sym toms in sexuel partner
Itraconazole (Sporanox) 100 mg cap $9 50 10 mg/ml oral solution (fasting state) (150 ml $147) *(AAC 42 1862 1998)* IV usual dose 200 mg bid x4 doses followed by 200 mg qd for a maximum of 14 days ($222/250 mg)	**itraconazole tablet and solution forms are not interchangeable, solution preferred.** Meny authorities recommend measuring drug serum concentration after 2 wks on prolonged rx to ensured satisfactory absorption To obtain the highest plasma concentration the tablet is given with food and acidic drinks (e g cole) while the solution is taken in the fested state under these conditions the peak conc of the capsule is approx 3 µg/ml and of the solution 5 4 µg/ml Peak levels are reached faster (2 2 vs 5 hrs) with the solution **Peak plasma concentrations after IV injection (200 mg) compared to oral capaula (200 mg): 2.8 µg/ml (on day 7 of rx) va 2 µg/mi (on day 36 of rx).** Protein-binding for both preparations is over 99% which explains the virtual absence of penetretion into the CSF **(do not use to treat meningitis)** Most common adverse effects are dose-releted nausea 10% diarrhea 8% vomiting 6% and abdominal discomfort 5 7% Allergic rash 8 6% ↑ bilirubin 6% edema 3 5% and hepatitis 2 7% reported ↑ doses may produce hypokalemia 8% and ↑ blood pressure 3 2% Thrombocytopenia and leukopenia reported *(AnIM 125 157, 1996)* Delirium reported *(Psychosomatics 44 260 2003)* **Reported to produce impairment in cardiac function** *(see footnote 3 page 78)* Other concern as with fluconazole and ketoconazole, is **drug-drug interactions; see *Tebla 22*** Some interactions can be life threatening
Ketoconazole (Nizoral) 200 mg tab $3 50	Gastric acid required for absorption—cimetidine, omeprazole antacids block absorption In achlorhydria dissolve tablet in 4 ml 0 2N HCl drink with a straw Coca-Cola ↑ absorption by 65% *(AAC 39 1671 1995)* CSF levels none' **Drug-drug interactions important, see *Teble 22* Soma interactions can be lite-threatening. Dose- dependent nausae end vomiting.** Liver toxicity of hepatocellular type reported in about 1 10 000 exposed pts—usually after several days to weeks of exposure At doses of ≥800 mg/d serum testosterone and plasma cortisol levels fall With high doses, adrenal (Addisonian) crisis reported
Miconazole (Monistat IV) 200 mg—*not available in U S*	IV miconazole indicated in patient critically ill with Pseudallescheria boydii Very toxic due to vehicle needed to get drug into solution
Nyatatin (Mycostetin) 30 gm cream $6 500 000 u oral tab $0 36	Topical virtually no adverse effects Less effective than imidazoles and triazoles PO large doses give occasional GI distress and diarrhea
Terbinafine (Lamisil) 250 mg tab $10 50	Rare cases (8) of idiosyncratic & symptomatic hepatic injury and more rarely liver failure leading to death or liver transplantation reported in pts receiving terbinafine for onychomycosis Therefore the drug is **not recommended** for pts with **chronic or activa liver disaase** although hepatotoxicity may occur in pts with or without pre-existing disease Pretreatment screening of serum transaminases (ALT & AST) is advised & alternate rx used for those with abnormal levels Pts started on terbinafine should be warned about symptoms suggesting liver dysfunction (persistent nausea anorexia, fatigue vomiting RUQ pain jaundice dark urine or pale stools) It symptoms develop drug should be discontinued & liver function immediately evaluated In controlled trials changes in ocular lens and retine reported—clinical significance unknown Mejor drug-drug interaction is 100% ↑ in rate of clearance by rifampin AEs usually mild transient and rarely caused discontinuation of rx % with AE, terbinafine vs placebo nausea/diarrhea 2 6–5 6 vs 2 9 rash 5 6 vs 2 2 taste abnormality 2 8 vs 0 7 Inhibits CYP2D6 en zymes *see Table 22*
Voriconazole (Vfend) **IV: Loading dose 6 mg/kg q12h x1 d., then 4 mg/kg q12h iV** for invasive aspergillus & serious mold infections **3 mg/kg q12h IV** for serious candida infections **Oral: >40 kg body weight:** 400 mg po q12h x1 d then 200 mg po q12h **<40 kg body weight:** 200 mg po q12h x1 d then 100 mg po q12h **Take oral dose 1 hour batore or 1 hour after aating.** Qral suspension (40 mg/ml) $36 49/200 mg dose Qral suspension dosing Same as for oret tabs Reduce to ½ maintenance dose for moderate hepatic insufficiency	A triazole with activity against Aspergillus sp including Ampho resistant strains of A terreus *(JCM 37 2343 1999)* Active vs Candida sp (including krusei) Fusarium sp & various molds Steady state serum levels reach 2 5–4 µg/ml Toxicity similar to other azoles/triazoles including uncommon serious hepatic toxicity (hepatitis cholestasis & fulminant hepatic failure Liver function tests should be monitored during rx & drug dc'd if abnormalities develop Rash reported in up to 20% occ photosensitivity & rare Stevens-Johnson hallucinations & anephylactoid infusion reactions with fever and hypertension *(Clin Exp Dermatol 26 648 2001)* 1 case of QT prolongation with ventricular tachycardia in e 15 y/o pt with ALL reported *(CID 39 884 2004)* **Approx. 30% experience a transient visual diaturbanca** following IV or po ("altered/enhanced visual perception", blurred or colored visual change or photophobia) within 30–60 minutes Visual changes resolve within 30–60 min after administration & are attenueted with repeated doses (**do not drive at night tor outpetient rx**) No persistence of effect reported Cause unknown In patients with CtCr <50 ml/min the drug should be given orally, not IV, since the intravenous vehicle (SBECD-sulfobutylether-B cyclodextrin) may accumulate Potential for drug-drug interections high—*see Table 22 (CID 36 630 1087, 1122 2003)* **NOTE:** Not in urine in active form **Coet:** 50 mg tab $9 200 mg tab $35 200 mg IV $109

* From 2004 Drug Topics Red Book Medical Economics Data and Hospital Formulary Pricing Guide **Price is averege wholesale price (AWP).**

See page 81 for abbreviations *All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function*

TABLE 12A: TREATMENT OF MYCOBACTERIAL INFECTIONS*

Tuberculin skin test (TST). Same as PPD *(MMWR 52(RR-2) 15, 2003)*
Criteria for positive TST after 5 tuberculin units (intermediate PPD) read at 48–72 hours
≥5 mm induration + HIV immunosuppressed <15 mg prednisone/day healed TBc on chest x ray recent close contact
≥10 mm induration foreign-born countries with high prevalence IVDUsers low income NH residents chronic illness silicosis
≥15 mm induration otherwise healthy
Two-stage to detect sluggish positivity If 1st PPD pos but <10 mm repeat intermediate PPD in 1 week Response to 2nd PPD can also happen if pt received BCG in childhood
BCG vaccine as child if ≥10 mm induration & from country with TBc should be attributed to M. tuberculosis Prior BCG may result in booster effect in 2-stage TST *(ArIM 161 1760 2001)*
Routine anergy testing no longer recommended in HIV+ or HIV-negative patients *(JAMA 283 2003 2000)*
Whole blood interferon-gamma release assay [QuantiFERON-TB (OFT)] approved by U S FDA as diagnostic test for TB *(JAMA 286 1740 2001, CID 34 1449 & 1457, 2002)* CDC recommends TST for tuberculosis suspects & pts at ↑ risk for progression to active TB & suggests either TST or OFT for individuals at ↑ risk for latent TB (LTBI) & for persons who warrant testing but are deemed at low risk for LTBI *(MMWR 52(RR-2) 15 2003)* An extremely sensitive enzyme-linked immunospot method (ELISpot) using antigens specific for MTB (do not cross-react with BCG) is under evaluation & looks promising *(Thorax 58 916, 2003, Ln 361 1168, 2003, AeIM 140 709, 2004)*

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: INITIAL THERAPY	SUGGESTED REGIMENS: CONTINUATION PHASE OF THERAPY
I. Mycobacterium tuberculosis expoaura but TST negative (household members & other close contacts of potentially infectious cases)	Neonate—Rx essential	INH (10 mg/kg/day for 3 months)	Repeat tuberculin skin test (TST) in 3 mos If mother s smear negative & infant s TST negative & chest x-ray (CXR) normal stop INH In UK BCG is then given *(Ln 2 1479, 1990)* unless mother HIV+ If infant s repeat TST positive &/or CXR abnormal (hilar adenopathy &/or infiltrate) INH + RIF (10–20 mg/kg/day) (or SM) Total rx 6 months If mother is being rx separation of infant from mother not indicated
	Children <5 years of age—Rx indicated	As for neonate for 1st 3 months	If repeat TST at 3 months is negative stop If repeat TST positive continue INH for total of 9 months If INH not given initially repeat TST at 3 mos if positive rx with INH for 9 mos *(see Category II below)*
	Older children & adults—Risk 2–4% 1st year	No rx	

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: INITIAL THERAPY	SUGGESTED REGIMENS: ALTERNATIVE
II. Treatment of latent infection with M. tuberculosis (formarly known as "prophylaxia) *(AJRCCM 161 S221 2000 NEJM 347 1860, 2002 NEJM 350 2060 2004)* **A. INH indicated due to high-risk** Assumes INH susceptibility likely INH 54–88% effective in preventing active TB for ≥20 years	(1) + tuberculin reactor & HIV+ (risk of active disease 10%/yr AIDS 170x ↑ HIV+ 113x ↑)* Development of active TBc in HIV+ pts after INH usually due to reinfection not INH failure *(CID 34 386 2002)* (2) Newly infected persons (TST conversion in past 2 yrs— risk 3 3% 1st yr) (3) Past tuberculosis not rx with adequate chemotherapy (INH RIF or alternatives) (4) + tuberculin reactors with CXR consistent with non-progressive tuberculous disease (risk 0 5–5 0%/yr) (5) + tuberculin reactors with specific predisposing conditions illicit injection drug use *(MMWR 38 236 1989)* silicosis diabetes mellitus prolonged adrenocorticoid rx (>15 mg prednisone/day) immunosuppressive rx hematologic diseases (Hodgkin s leukemia) endstage renal disease clinical condition with substantial rapid weight loss or chronic under-nutrition previous gastrectomy *(AARD 134 355 1986)* *** NOTE: For HIV, see SANFORD GUIDE TO HIV/AIDS THERAPY and/or MMWR 48:RR-10, 1999**	**INH** (5 mg/kg/d maximum 300 mg/d for adults 10 mg/kg/d not to exceed 300 mg/d for children) May use twice-weekly INH with DOT *(MMWR 52 735 2003)* Optimal duration 9 mos (includes children HIV–, HIV+ old fibrotic lesions on chest x ray) In some cases, 6 mos may be given for cost effectiveness *(AJRCCM 161 S221 2000)* Do not use 6 mo regimen in HIV+ persons <18 yrs old or those with fibrotic lesions on chest film *(NEJM 345 189 2001)*	If compliance problem **INH** by DOT† 15 mg/kg 2x/wk x9 mos 2-month **RIF + PZA** regimen effective in HIV– and HIV+ *(AJRCCM 161 S221 2000 JAMA 283 1445 2000)* **However, there are recent deacriptiona of savere & fatal hepatitis in pta on RIF + PZA** *(MMWR 50 289, 2001)* Therefore this regimen is no longer recommended for LTBI *(MMWR 52 735 2003)* **RIF** 600 mg/d po for 4 mos (HIV– and HIV+)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: INITIAL THERAPY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
B. TST positiva (organisma likaly to be INH-auscaptibla)	Age no longer considered modifying factor *(see Comments)*	**INH** (5 mg/kg/d max 300 mg/d for adults 10 mg/kg/d not to exceed 300 mg/d for children) Results with 6 mos rx not quite as effective as 12 mos (65% vs 75% reduction in disease) 9 mos is current recommendation *See IIA above for details and alternate rx*	Reanalysis of earlier studies favors **INH** prophylaxis (if INH related hepatitis case fatality rate <1% and TB case fatality >6 7% which appears to be the case) *(ArIM 150 2517 1990)* Recent data suggest INH prophylaxis has positive risk-benefit ratio in pts ≥35 if monitored for hepatotoxicity *(AIM 127 1051 1997)* Overall risk of hepatotoxicity 0 1–0 15% *(JAMA 281 1014 1999)*	

See pages 90 & 92 for abbreviations page 88 for footnotes * *Dosages are for adults (unless otherwise indicated) and assume normal renal function* † **DOT** directly observed therapy

TABLE 12A (2)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: INITIAL THERAPY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
II Treatment of latent infection with M. tuberculosis ("prophylaxis")/TST positive (organisms likely to be susceptible) *(continued)*				
	Pregnancy—Any risk factors *(II A above)*	Treat with **INH** as above For women at risk for progression of latent to active disease esp those who are HIV+ or who have been recently infected, rx should not be delayed even during the first trimester		Risk of INH hepatitis may be ↑ *(Ln 346 199, 1995)*
	Pregnancy—No risk factors	No initial rx *(see Comment)*		Delay rx until after delivery *(AJRCCM 149 1359, 1994)*
C. TST positive & drug resistance likely (For data on worldwide prevalence of drug resistance see *NEJM 344 1294, 2001 JID 185 1197, 2002)*	INH-resistant (or adverse reaction to INH) RIF-sensitive organisms likely	**RIF** 600 mg/d po for 4 mos (HIV+ or HIV-)		IDSA guideline lists rifabutin in 600 mg/d dose as another alternative however current recommended max dose of rifabutin is 300 mg/d Estimate RIF alone has protective effect of 56% 26% of pts reported adverse effects (only 2/157 did not complete 6 mos rx) *(AJRCCM 155 1735, 1997)*
	INH and RIF resistant organisms likely	Efficacy of all regimens unproven (**PZA** 25–30 mg/kg/d to max of 2 gm/d + **ETB** 15–25 mg/kg/d po) x6–12 mos	[(**PZA** 25 mg/kg/d to max of 2 0 gm/d) + (**levoflox** 500 mg/d or **oflox** 400 mg bid)] all po x6–12 mos	PZA + oflox has been associated with asymptomatic hepatitis *(CID 24 1264 1997)*

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUM-STANCES	SUGGESTED REGIMENS: INITIAL PHASE[a]			SUGGESTED REGIMENS: CONTINUATION PHASE OF THERAPY[a] (in vitro susceptibility known)			
		SEE COMMENTS FOR DOSAGE AND DIRECTLY OBSERVED THERAPY (DOT) REGIMENS						
		Regimen: in order of preference	Drugs	Interval/Doses[1] (min. duration)	Regimen	Drugs	Interval/Doses[1,2] (min. duration)	Range of Total Doses (min. duration)
III Mycobacterium tuberculosis A. Pulmonary TB *[General reference on rx in adults & children Ln 362 887 2003 MMWR 52(RR-11) 1 2003]*	Rate of INH resistance known to be <4% (drug susceptible organisms) *[Modified from MMWR 52(RR-11) 1 2003]*	1 *(See Fig 1 page 87)*	INH RIF PZA ETB	7 d/wk x56 doses (8 wk) or 5 d/wk x40 doses (8 wk)[3]	1a	INH/RIF	7 d/wk x126 doses (18 wk) or 5 d/wk x90 doses (18 wk)[3]	182–130 (26 wk)
					1b	INH/RIF	2x/wk x36 doses (18 wk)	92–76 (26 wk)[4]
					1c[5]	INH/RFP	1x/wk x18 doses (18 wk)	74–58 (26 wk)
		2 *(See Fig 1, page 87)*	INH RIF PZA ETB	7 d/wk x14 doses (2 wk) then 2x/wk x12 doses (6 wk) or 5 d/wk x10 doses (2 wk)[3] then 2x/wk x12 doses (6 wk)	2a	INH/RIF	2x/wk x36 doses (18 wk)	62–58 (26 wk)[4]
					2b[5]	INH/RFP	1x/wk x18 doses (18 wk)	44–40 (26 wk)
		3 *(See Fig 1, page 87)*	INH RIF PZA ETB	3x/wk x24 doses (8 wk)	3a	INH/RIF	3x/wk x54 doses (18 wk)	78 (26 wk)
		4 *(See Fig 1, page 87)*	INH RIF ETB	7 d/wk x56 doses (8 wk) or 5 d/wk x40 doses (8 wk)[3]	4a	INH/RIF[6]	7 d/wk x217 doses (31 wk) or 5 d/wk x155 doses (31 wk)[3]	273–195 (39 wk)
					4b	INH/RIF[6]	2x/wk x62 doses (31 wk)	118–102 (39 wk)

Isolation essential! Pts with active TB should be isolated in single rooms not cohorted Older observations on infectivity of susceptible & resistant M tbc before and after rx *(ARRD 85 5111 1962)* may not be applicable to MDR M tbc or to the HIV+ individual Extended isolation may be appropriate

See footnotes, page 88

USE DOT REGIMENS IF POSSIBLE

(continued on next page)

COMMENTS

Dose in mg/kg (max. daily dose)

Regimen*	INH	RIF	PZA	ETB	SM	RFB
Daily						
Child	10–20 (300)	10–20 (600)	15–30 (2000)	15–25	20–40 (1000)	10–20 (300)
Adult	5 (300)	10 (600)	15–30 (2000)	15–25	15 (1000)	5 (300)
2x/wk (DOT)						
Child	20–40 (900)	10–20 (600)	50–70 (4000)	50	25–30 (1500)	10–20 (300)
Adult	15 (900)	10 (600)	50–70 (4000)	50	25–30 (1500)	5 (300)
3x/wk (DOT)						
Child	20–40 (900)	10–20 (600)	50–70 (3000)	25–30	25–30 (1500)	NA
Adult	15 (900)	10 (600)	50–70 (3000)	25–30	25–30 (1500)	NA

Second-line anti TB agents can be dosed as follows to facilitate DOT Cycloserine 500–750 mg qd (5x/wk) po
Ethionamide 500–750 mg qd (5x/wk) po
Kanamycin or capreomycin 15 mg/kg qd (3–5x/wk) IM/IV
Ciprofloxacin 750 mg qd (5x/wk) po
Ofloxacin 600–800 mg qd (5x/wk) po
Levofloxacin 750 mg qd (5x/wk) po *(CID 21 1245 1995)*

Risk factors for drug-resistant TB Recent immigration from Latin America or Asia or living in area of ↑ resistance (≥4%) or previous rx without RIF exposure to known MDR TB Incidence of MDR TB in U S appears to have stabilized and may be slightly decreasing in early 1990s *(JAMA 278 833 1997)* Incidence of primary drug resistance is particularly high (>25%) in parts of China Thailand Russia, Estonia & Latvia *(NEJM 344 1294, 2001, NEJM 347 1850 2002)* *(continued on next page)*

See pages 90 & 92 for abbreviations, page 88 for footnotes

[a] *Dosages are for adults (unless otherwise indicated) and assume normal renal function*

[i] **DOT** = directly observed therapy

TABLE 12A (3)

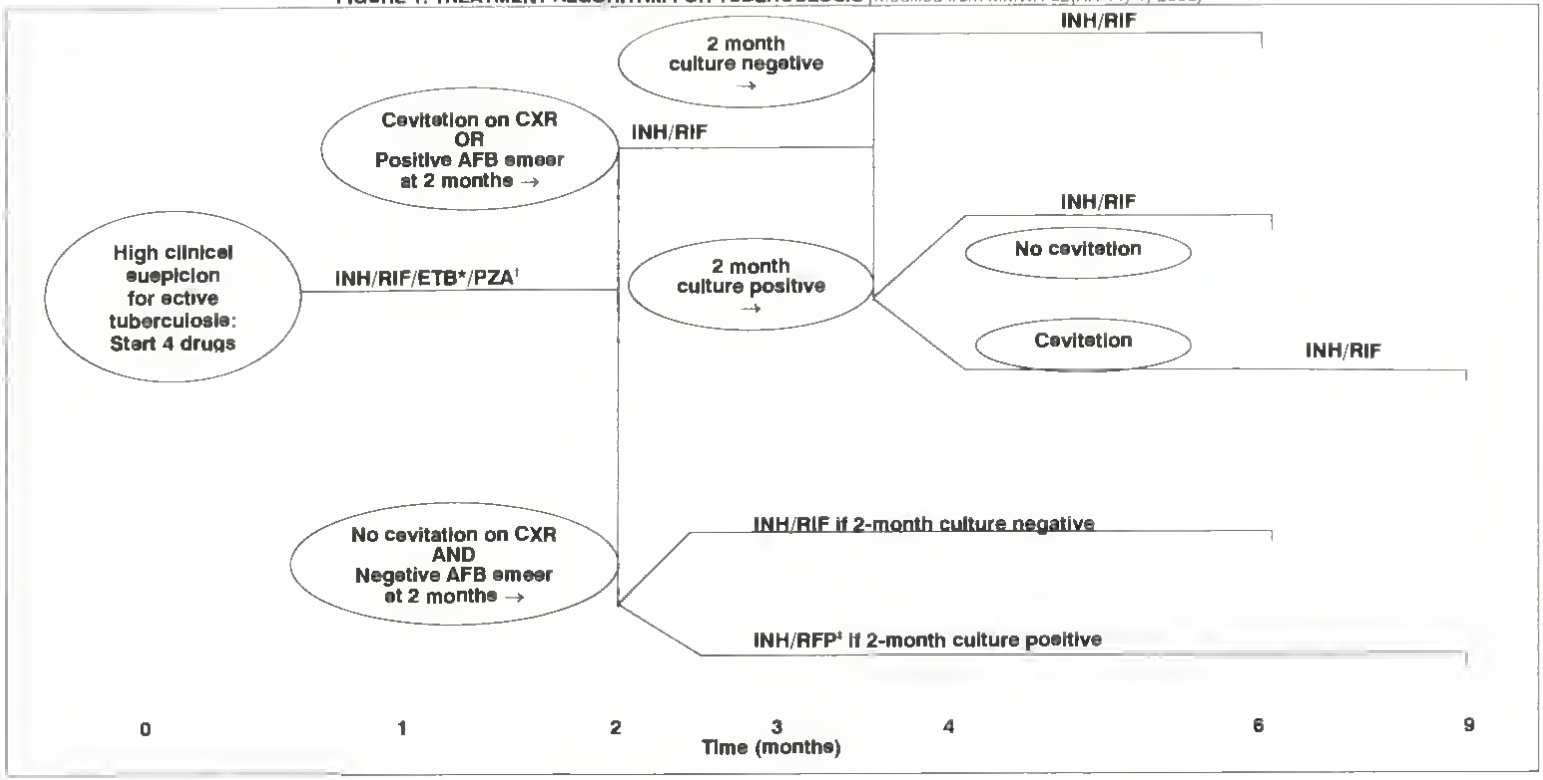
CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUM-STANCES	SUGGESTED REGIMEN[5]	DURATION OF TREATMENT (mo.)[6]	SPECIFIC COMMENTS[5]	COMMENTS
III. Mycobacterium tuberculosis **A. Pulmonary TB** *(continued from previous page)* REFERENCE *CID 22 683 1996*	INH (± SM) resistance	**RIF PZA ETB** (an **FQ** may strengthen the regimen for pts with extensive disease) Emergence of FD resistance a concern *(LnID 3 432, 2003)*	6	In British Medical Research Council trials 6-mo regimens have yielded ≥95% success rates despite resistance to INH if 4 drugs were used in the initial phase & RIF + ETB or SM was used throughout *(ARRD 133 423 1986)* Additional studies suggested that results were best if PZA was also used throughout the 6 mos *(ARRD 136 1339 1987)* FOs were not employed in BMRC studies but may strengthen the regimen for pts with more extensive disease INH should be stopped in cases of INH resistance *[see MMWR 52(RR-11) 1 2003 for additional discussion]*	*(continued from previous page)* For MDR TB consider rifabutin (~30% RIF-resistant strains are rifabutin-susceptible) Note that CIP not as effective as PZA + ETB in multidrug regimen for susceptible TB *(CID 22 287, 1996)* Moxifloxacin gatifloxacin and levofloxacin have enhanced activity compared with CIP against M tuberculosis *(AAC 46 1022, 2002 AAC 47 2442 2003 AAC 47 3117, 2003 JAC 53 441 2004 AAC 48 780 2004)* FQ resistance may be seen in pts previously treated with FO *(CID 37 1448 2003)* Linezolid has excellent in vitro activity including MDR strains *(AAC 47 416, 2003)* Mortality reviewed *Ln 349 71 1997* Rapid (24-hr) diagnostic tests for M tuberculosis (1) the Amplified Mycobacterium tuberculosis Direct Test amplifies and detects M tuberculosis ribosomal RNA (2) the AMPLICOR Mycobacterium tuberculosis Test amplifies and detects M tuber culosis DNA Both tests have sensitivities & specificities >95% in sputum samples that are AFB-positive In negative smears specificity remains >95% but sensitivity is 40–77% *(AJCCM 155 1497 1997)* Note that MTB may grow out on standard blood agar plates in 1–2 wks *(JCM 41 1710 2003)*
Multidrug-Resistant Tuberculosis (MDR TB) Defined as resistant to at least 2 drugs Pt clusters with high mortality *(AnIM 118 17, 1993, EJCMID 23 174, 2004)*	Resistance to INH & RIF (± SM)	**FO PZA ETB IA** ± alternative agent[7]	18–24	In such cases extended rx is needed to ↓ the risk of relapse In cases with extensive disease the use of an additional agent (alternative agents) may be prudent to ↓ the risk of failure & additional acquired drug resistance Resectional surgery may be appropriate	
	Resistance to INH RIF (± SM) & ETB or PZA	**FO** (**ETB** or **PZA** if active) **IA** & 2 alternative agents[7]	24	Use the first-line agents to which there is susceptibility Add 2 or more alternative agents in case of extensive disease Surgery should be considered Survival ↑ in pts receiving active FO & surgical intervention *(AJRCCM 169 1103, 2004)*	
See footnotes, page 88	Resistance to RIF	**INH ETB FQ** supplemented with **PZA** for the first 2 mos (an IA may be included for the first 2–3 mos for pts with extensive disease)	12–18	Daily & 3x/wk regimens of INH PZA & SM given for 9 mos were effective in a BMRC trial *(ARRD 115 727 1977)* However extended use of an IA may not be feasible It is not known if ETB would be as effective as SM in these regimens An all-oral regimen x12–18 mos should be effective But for more extensive disease &/or to shorten duration (e g to 12 mos) an IA may be added in the initial 2 mos of rx	

CAUSATIVE AGENT/DISEASE; MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: INITIAL THERAPY	SUGGESTED REGIMENS: CONTINUATION PHASE OF THERAPY (In vitro susceptibility known)	COMMENTS
B. Extrapulmonary TB	**INH** + **RIF** (or **RFB**) + **PZA** daily x2 months	**INH** + **RIF** (or **RFB**)	6-month regimens probably effective Most experience with 9–12 month regimens Am Acad Ped (1994) recommends 6 mos rx for isolated cervical adenitis renal and 12 mos for meningitis miliary bone/joint DOT useful here as well as for pulmonary tuberculosis IDSA recommends 6 mos for lymph node pleural pericarditis, disseminated disease genitourinary & peritoneal TBc, 6–9 mos for bone & joint 9–12 mos for CNS (including meningeal) TBc Corticosteroids "strongly recommended" only for pericarditis & meningeal TBc *[MMWR 52(RR-11) 1, 2003]*
	Authors add **pyridoxine** 25–50 mg po daily to regimens that include INH		
C. Tuberculous meningitis *For critical appraisal of adjunctive steroids CID 25 872 1997*	**INH** + **RIF** + **ETB** + **PZA**	May omit ETB when susceptibility to **INH** and **RIF** established *See Table 9 page 60 for CSF drug penetration*	3 drugs often recommended for initial rx we prefer 4 May substitute ethionamide for ETB Infection with MDR TB ↑ mortality & morbidity *(CID 38 851 2004)* Dexamethasone (for 1st month) has been shown to ↓ complications *(Pediatrics 99 226, 1997)* PCR of CSF markedly increases diagnostic sensitivity and provides rapid dx *(Neurol 45 2228 1995 Arch Neurol 53 771 1996)* but considerable variability in sensitivity depending on method used *(LnID 3 633, 2003)*
D. Tuberculosis during pregnency	**INH** + **RIF** + **ETB** for 9 months		PZA not recommended teratogenicity data inadequate Because of potential ototoxicity to fetus throughout gestation (16%) SM should not be used unless other drugs contraindicated Add pyridoxine 25 mg/kg/d for pregnant women on INH Breast-feeding should not be discouraged in pts on first-line drugs *[MMWR 52(RR 11) 1, 2003]*
E. Treatment failure or relapse: Usually due to poor compliance or resistant organisms *(AJM 102 164 1997)*	Directly observed therapy (DOT) Check susceptibilities *(See section III A page 85 & above)*		Patients whose sputum has not converted after 5–6 mos = treatment failures Failures may be due to non-compliance or resistant organisms Check susceptibilities of original isolates and obtain susceptibility on current isolates Non-compliance common therefore institute DOT If isolates show resistance modify regimen to include at least 2 effective agents preferably ones which patient has not received Surgery may be necessary In HIV+ patients reinfection is a possible explanation for ↑ failure

See pages 90 & 92 for abbreviations page 88 for footnotes * *Dosages are for adults (unless otherwise indicated) and assume normal renal function* † **DOT** = directly observed therapy

TABLE 12A (4)

FIGURE 1: TREATMENT ALGORITHM FOR TUBERCULOSIS *[Modified from MMWR 52(RR-11) 1, 2003]*



If the pt has HIV infection & the CD4 cell count is <100/μl, the continuation phase should consist of daily or 3x/wk INH & RIF for 4–7 months.
*** ETB may be discontinued in <2 months if drug susceptibility testing indicate no drug resistance. † PZA may be discontinued after 2 months (56 doses). ‡ RFP should not be used in HIV patients with tuberculosis or in patients with extrapulmonary tuberculosis.**

See pages 90 & 92 for abbreviations, page 88 for footnotes

** Dosages are for adults (unless otherwise indicated) and assume normal renal function*

† **DOT** = directly observed therapy

TABLE 12A (5)

CAUSATIVE AGENT/DISEASE	MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS PRIMARY/ALTERNATIVE	COMMENTS
III. Mycobacterium tuberculosis *(continued)*			
F. HIV infection or AIDS—pulmonary or extrapulmonary	**INH** + **RIF** (or **RFB**) + **PZA** daily x2 months	**INH** + **RIF** (or **RFB**) daily x4 months (total 6 mos) May treat up to 9 mos in pts with delayed response (Authors add **pyridoxine** 25–50 mg po daily to regimens that include INH)	1 Because of the possibility of developing resistance to RIF in pts with low CD4 cell counts who receive weekly or biweekly doses of RFB, it is recom that such pts receive daily (or minimally 3x/ weekly) doses of RFB for initiation & continuation phase of rx *(MMWR 51 214 2002)* 2 Clinical and microbiologic response same as in HIV-negative patient although there is considerable variability in outcomes among currently available studies *(CID 32 623, 2001)* 3 Post-treatment suppression not necessary for drug-susceptible strains 4 Rate of INH resistance known to be <4% (for ↑ rates of resistance see *Section III A*) 5 For more information see *MMWR 47(RR-20) 1 1998 CID 28 139, 1999, MMWR 52(RR-11) 1 2003* 6 May use partially intermittent therapy 1 dose/day for 2 weeks followed by 2–3 doses/week for 24 weeks *[MMWR 47(RR-20), 1998]*
Concomitant protease inhibitor (PI) therapy *(Modified from MMWR 49 185 2000, AJRCCM 162 7 2001)*	**Initial & cont. therapy:** **INH** 300 mg + **RFB** *(see below for dose)* + **PZA** 25 mg/kg + **ETB** 15 mg/kg daily x2 mos then **INH** + **RFB** x4 mos (up to 7 mos) **PI Regimen** / **RFB Dose** Nelfinavir 1200 mg q12h or indinavir 1000 mg q8h or amprenavir 1200 mg q12h — 150 mg qd or 300 mg intermittently Lopinavir/ritonavir—standard dose — 150 mg 2x/wk	**Alternative regimen:** **INH** + **SM** + **PZA** + **ETB** x2 mos , then **INH** + **SM** + **PZA** 2–3 times/ wk for 7 mos May be used with any PI regimen May be prolonged up to 12 mos in pts with delayed response	**Comments:** Rifamycins induce cytochrome CYP450 enzymes (RIF > RFP > RFB) & reduce serum levels of concomitantly administered PIs Conversely PIs (ritonavir > amprenavir > indinavir = nelfinavir > saquinavir) inhibit CYP450 & cause ↑ serum levels of RIF, RFP & RFB If dose of RFB is not reduced, toxicity ↑ **Do not use RIF + PI** RFB/PI combinations are therapeutically effective *(CID 30 779 2000)* RFB has no effect on nelfinavir levels at dose of 1250 mg bid *(Can JID 10 218 1999)*

FOOTNOTES: [1] When DOT is used drugs may be given 5 d/wk & the necessary number of doses adjusted accordingly Although there are no studies that compare 5 with 7 daily doses extensive experience indicates this would be an effective practice [2] Patients with cavitation on initial chest x-ray & positive cultures at completion of 2 months of rx should receive a 7-month (31 wk either 217 doses [daily] or 62 doses [2x/wk] continuation phase [3] 5-day a wk administration is always given by DOT [4] Not recommended for HIV-infected pts with CD4 cell counts <100 cells/µl [5] Options 1c & 2b should be used only in HIV-neg pts who have neg sputum smears at the time of completion of 2 months of rx & who do not have cavitation on initial chest x-ray For pts started on this regimen & found to have a pos culture from the 2-month specimen, rx should be extended an extra 3 months [6] Options 4a & 4b should be considered only when options 1–3 cannot be given [7] Alternative agents = ethionamide cycloserine p-aminosalicylic acid clarithromycin AM/CL linezolid [8] Modified from *MMWR 52(RR-11) 1, 2003 See also IDCP 11 329 2002*

IV. Other Mycobacterial Diseases ("Atypical") *(See ATS Consensus AJRCCM 152 51 1997 IDC No Amer March 2002 CMR 15 716, 2002)*			
A. M. bovis		**INH + RIF + ETB**	The M tuberculosis complex includes M bovis All isolates resistant to PZA 9–12 months of rx used by some authorities Isolation not required
B. Bacillus Calmette-Guerin (BCG) (derived from M bovis)	Only fever (>38 5 C) for 12–24 hrs	**INH** 300 mg qd x3 months	Intravesical BCG effective in superficial bladder tumors and carcinoma in situ Adverse effects fever 2 9% granulomatosis pneumonitis hepatitis 0 7%, sepsis 0 4% *(J Urol 147 596 1992)* With sepsis consider initial adjunctive prednisolone Resistant to PZA
	Systemic illness or sepsis	(**INH** 300 mg) + (RIF 600 mg) + (**ETB** 1200 mg) qd po x6 mos	
C. M. avium-intracellulare complex (MAC MAI or Battey bacillus) ATS Consensus Statement *AJRCCM 156 51 1997 Clin Chest Med 23 633 2002*	**Immunocompetent patients** with chronic pulmonary, disseminated disease (subcutaneous, bone)	**Clarithro** 500 mg po bid (or **azithro** 600 mg po qd) + **ETB** 25 mg/kg po x2 mos then 15 mg/kg po + **RIF** 600 mg po qd (or **RFB** 300 mg po qd) May add **SM** or **AMK** 15 mg/kg tiw for 2–6 mos for severe disease May also add **CLO** 100–200 mg po qd (until 'tan then 50 mg po qd or 100 mg po tiw) Rx until culture neg x1 yr Alternative **Clarithro** 500 mg po bid + **ETB** 15–25 mg/kg po qd + **RFB** 300 mg po qd for up to 24 mos *(Curr Inf Dis Repts 2 193, 2000, CID 32 1547 2001)* Regimens dosing azithro 600 mg tiw also effective *(CID 32 1547 2001)*	**"Classic" pulmonary MAC:** Men 50–75 smokers COPD May be associated with hot tub use *(Clin Chest Med 23 675, 2002)* **"New" pulmonary MAC:** Women 30–70 scoliosis, mitral valve prolapse (bronchiectasis) pectus excavatum (Lady Windermere syndrome) May also be associated with interferon gamma deficiency *(AJM 113 756, 2002)* Susceptibility testing of MAC not recommended except clarithro testing of isolates from pts who have failed prior clarithro rx 3x/wk azithro (600 mg po) ETB (25 mg/kg po) RFB (600 mg po) & initial 2x/wk SM may be effective in immunocompetent patients *(JID 178 121 1998 CID 30 288, 2000)* Late 'relapses (following completion of therapy) after treatment with clarithro or azithro in pts with nodular bronchiectasis usually represent reinfection not failure of rx *(JID 186 266 2002)*

See pages 90 & 92 for abbreviations page 88 for footnotes * *Dosages are for adults (unless otherwise indicated) and assume normal renal function* ' **DOT** directly observed therapy

CAUSATIVE AGENT/DISEASE; MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
19. Other Mycobacteria Causing Atypical *(continued)*			
C. M. avium-intracellulare complex *(continued)*	**Immunocompromised pts:** **Primary prophylaxis**—Pts CD4 count <50–100/mm³ Discontinue when CD4 count >100/mm³ in response to HAART *(NEJM 342 1085, 2000 CID 34 662, 2002)* Guideline *AnIM 137 435, 2002*	**PRIMARY**	**ALTERNATIVE**	**COMMENTS**
		Azithro 1200 mg po weekly OR **Clerithro** 500 mg po bid	**RFB** 300 mg po qd OR **Azithro** 1200 mg po weekly + **RIF** 300 mg po qd	RFB reduces MAC infection rate by 55% (no survival benefit) clarithro by 68% (30% survival benefit) azithro by 59% (68% survival benefit) *(CID 26 611 1998)* Azithro + RFB more effective than either alone but not as well tolerated *(NEJM 335 392 1996)* **Many drug-drug interactions,** *see Table 22 pages 145 147* Drug-resistant MAI disease seen in 29–58% of pts in whom disease develops while taking clarithro prophylaxis & in 11% of those on azithro but has not been observed with RFB prophylaxis *(J Inf 38 6 1999)* Clarithro resistance more likely in pts with extremely low CD4 counts at initiation *(CID 27 807 1998)* Need to be sure no active M tbc RFB used for prophylaxis may promote selection of rifamycin-resistant M tbc *(NEJM 335 384 & 428 1996)*
	Treatment Either presumptive dx or after positive culture of blood bone marrow or other usually sterile body fluids e g liver	(**Clerithro** 500 mg* po bid or **azithro** 600 mg po qd) + **ETB** 15–25 mg/kg/d + **RFB** 300 mg po qd ***Higher dosas of clari (1000 mg bid) may be asaociated with ↑ mortality** *(CID 29 125, 1999)*	**Clarithro** or **azithro** + **ETB** + **RFB** + one or more of **CIP** 750 mg po bid **Oflox** 400 mg po bid **Amikacin** 7 5–15 mg/kg IV qd In pts receiving protease inhibitors can use (**clarithro** 500 mg bid (or **azithro** 600 mg qd) + **ETB** 15–25 mg/kg/d] if the pt has not had previous prophylaxis with a neomacrolide *(Johns Hopkins AIDS Report 9 2 1997)*	Median time to neg blood culture clarithro + ETB 4 4 wks vs azithro + ETB >16 wks At 16 wks clearance of bacteremia seen in 37 5% of azithro- & 85 7% of clarithro-treated pts *(CID 27 1278 1998)* More recent study suggests similar clearance rates for azithro (46%) vs clarithro (56%) at 24 wks when combined with ETB *(CID 31 1245 2000)* Azithro 250 mg po qd not effective but azithro 600 mg po qd as effective as 1200 qd & yields fewer adverse effects *(AAC 43 2869, 1999)* Addition of RFB to clarithro + ETB ↓ emergence of resistance to clari ↓ relapse rate & improves survival *(CID 37 1234 2003)* Data on clofazimine difficult to assess Earlier study suggested adding CLO of no value *(CID 25 621 1997)* More recent study suggests it may be as effective as RFB in 3 drug regimens containing clari & ETB *(CID 29 125, 1999)* although it may not be as effective as RFB at preventing clari resistance *(CID 28 136 1999)* Thus pending more data we still do not recommend CLO for MAI in HIV+ pts Drug toxicity With clarithro 23% pts had to stop drug 2° to dose-limiting adverse reaction *(AnIM 121 905, 1994)* Combination of clarithro ETB and RFB led to uveitis and pseudojaundice *(NEJM 330 438 1994)* result is reduction in max dose of RFB to 300 mg Treatment failure rate is high Reasons drug toxicity development of drug resistance & inadequate serum levels Serum levels of clarithro ↓ in pts also given RIF or RFB *(JID 171 747 1995)* If pt not responding to initial regimen after 2–4 weeks add one or more drugs Several anecdotal reports of pts not responding to usual primary regimen who gained weight and became afebrile with dexamethasone 2–4 mg/d po *(AAC 38 2215, 1994 CID 26 682, 1998)*
	Chronic post-treatment suppression—secondary prophylaxis	**Always necessary.** [**Clarithro** or azithro] + **ETB** (lower dose to 15 mg/kg/d *(dosage above)*	**Clerithro** or **azithro** + **RFB** *(dosage above)*	Recurrences almost universal without chronic suppression However in patients on HAART with robust CD4 cell response it may be possible to discontinue chronic suppression *(JID 178 1446, 1998, NEJM 340 1301, 1999)*
D. Mycobacterium celetum	Treatment optimal regimen not defined	May be susceptible to **clarithro FQ** *(Clin Microbiol Inf 3 582, 1997)* Suggest rx "like MAI but often resistant to RIF *(J Inf 38 157, 1999)* Most reported cases received 3 or 4 drugs usually clarithro + ETB + CIP ± RFB *(EID 9 399, 2003)*		Isolated from pulmonary lesions and blood in AIDS patients *(CID 24 144 1997)* Easily confused with M xenopi (and MAC) Susceptibilities similar to MAC but highly resistant to RIF *(CID 24 140 1997)*
E. Mycobacterium chelonae asp. abscessus **Mycobacterium chelonae asp. chelonae**	Treatment Surgical excision may facilitate clarithro rx in subcutaneous abscess and is important adjunct to rx *(CID 24 1147, 1997)*	**Clerithro** 500 mg po bid x6 mos *(AnIM 119 482 1993 CID 24 1147, 1997, EJCMID 19 43 2000)* Azithro may also be effective For serious disseminated infections add tobramycin + IMP for 1st 2–6 wks *(CMR 15 716 2002)*		M abscessus susceptible to AMK (70%) clarithro (95%) cefoxitin (70%), CLO cefmetazole Single isolates of M abscessus often not associated with disease Clarithro-resistant strains now described *(JCM 39 2745, 2001)* M chelonae susceptible to AMK (80%), clarithro azithro, tobramycin (100%), IMP (60%), gatifloxacin (90%) moxifloxacin *(AAC 46 3283 2002)* Resistant to cefoxitin, FQ *(CID 24 1147, 1997, AJRCCM 156 S1 1997)*
F. Mycobacterium fortuitum	Treatment optimal regimen not defined Surgical excision of infected areas	**AMK** + **cefoxitin** + **probenecid** 2–6 weeks then po **TMP/SMX** or **doxycycline** 2–6 mos Usually responds to 6–12 mos of oral rx with 2 drugs to which it is susceptible *(AAC 46 3283 2002 CMR 15 716, 2002)* Nail salon acquired infections respond to 4–6 mos of minocycline or doxy or CIP *(CID 38 38, 2004)*		**Resistant to all standard anti-TBc druga** Sensitive in vitro to doxycycline minocycline cefoxitin IMP AMK, TMP/SMX CIP oflox, azithro clarithro gatifloxacin (80%) *(AAC 46 3283, 2002)* linezolid *(CMR 15 716 2002)* May be resistant to azithromycin rifabutin *(JAC 39 567, 1997)*

TABLE 12A (7)

CAUSATIVE AGENT/DISEASE; MODIFYING CIRCUMSTANCES	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
IV. Other Mycobacterial Diseases ("Atypical") *(continued)*			
G. Mycobacterium haemophilum	Regimen(s) not defined. In animal model **clarithro** + **rifabutin** effective *(AAC 39 2316, 1995)*. Combination of **CIP** + **RFB** + **clarithro** reported effective but clinical experience limited *(CMR 9 435, 1996)*. Surgical debridement may be necessary *(CID 26 505, 1998)*		Clinical: Ulcerating skin lesions, synovitis, osteomyelitis. Lab: Requires supplemented media to isolate. Sensitive in vitro to CIP, cycloserine, rifabutin. Over ½ resistant to INH, RIF, ETB, PZA *(AnIM 120 118, 1994)*
H. Mycobacterium genavense	Regimens used include ≥2 drugs: **ETB**, **RIF**, **RFB**, **CLO**, **clarithro**. In animal model: **clarithro** & **RFB** (& to lesser extent amikacin & **ETB**) shown effective in reducing bacterial counts, CIP not effective *(JAC 42 483, 1998)*		Clinical: CD4 <50. Symptoms of fever, weight loss, diarrhea. Lab: Growth in BACTEC vials slow (mean 42 days). Subcultures grow only on Middlebrook 7H11 agar containing 2 µg/ml mycobactin J—growth still insufficient for in vitro sensitivity testing *(Ln 340 76, 1992, AnIM 117 586, 1992)*. Survival ↑ from 81 to 263 days in pts rx for at least 1 month with ≥2 drugs *(Arch Int Med 155 400, 1995)*
I. Mycobacterium gordonae	Regimen(s) not defined, but consider **RIF** + **ETB** + **KM** or **CIP** *(J Inf 38 157, 1999)*		In vitro: sensitive to ETB, RIF, AMK, CIP, clarithro, linezolid *(AAC 47 1736, 2003)*. Resistant to INH *(CID 14 1229, 1992)*. Surgical excision
J. Mycobacterium kansasii	Daily po **INH** (300 mg) + **RIF** (600 mg) + **ETB** (25 mg/kg x2 mos, then 15 mg/kg). Rx for 18 mos (until culture-neg sputum x12 mos, 15 mos if HIV+ pt) *(See Comment)*	If RIF-resistant: daily po **INH** (900 mg) + **pyridoxine** (50 mg) + ETB (25 mg/kg) + **sulfamethoxazole** (1.0 gm tid). Rx until pt culture-neg x12–15 mos *(See Comment)*. **Clari** + **ETB** + **RIF** also effective in small study *(CID 37 1178, 2003)*	Susceptibility testing: Test only RIF. Testing INH and streptomycin give misleading results. **All isolates are resistant to PZA.** Rifapentine, azithro, ETB effective alone or in combination in athymic mice *(JAC 42 417, 2001)*. Highly susceptible to linezolid in vitro *(AAC 47 1736, 2003)*. If HIV+ pt taking protease inhibitor, substitute either clarithro (500 mg bid) or RFB (150 mg/d) for RIF *(AJRCCM 156 S1, 1997)*. Because of variable susceptibility to INH, some substitute clarithro 500–750 mg daily for INH. However, resistance to clarithro reported *(DMID 31 369, 1998)*. Prognosis related to level of immunosuppression *(CID 37 584, 2003)*
K. Mycobacterium marinum	(**Clarithro** 500 mg bid) or (**minocycline** 100–200 mg qd) or (**doxycycline** 100–200 mg qd), or (**TMP/SMX** 160/800 mg po bid), or (**RIF** + **ETB**) for 3 mos *(AJRCCM 156 S1, 1997)*. Surgical excision		Resistant to INH & PZA *(AJRCCM 156 S1, 1997)*. Also susceptible in vitro to linezolid *(AAC 47 1736, 2003)*. CIP, gatifloxacin, moxifloxacin also show moderate in vitro activity *(AAC 46 1114, 2002)*
L. Mycobacterium scrofulaceum	Surgical excision. Chemotherapy seldom indicated. Although regimens not defined, **clarithro** + **CLO** with or **without ETB**, **INH**, **RIF**, **strep** + **cycloserine** have also been used		In vitro: resistant to INH, RIF, ETB, PZA, AMK, CIP *(CID 20 549, 1995)*. Susceptible to clarithro, strep, erythromycin
M. Mycobacterium simiae	Regimen(s) not defined. Start 4 drugs as for disseminated MAI		Most isolates resistant to all 1st-line anti-tbc drugs. Isolates often not clinically significant *(CID 26 625, 1998)*
N. Mycobacterium ulcerans (Buruli ulcer)	[**RIF** + **AMK** (7.5 mg/kg IM bid)] or [**ETB** + **TMP/SMX** (160/800 mg po tid)] for 4–6 weeks. Surgical excision		Susceptible in vitro to RIF, strep, CLO, clarithro, CIP, oflox, amikacin *(AAC 42 2070, 1998; JAC 45 231, 2000; AAC 46 3193, 2002)*. Monotherapy with RIF selects resistant mutants in mice *(AAC 47 1228, 2003)*. Treatment generally disappointing—see *review Ln 354 1013, 1999*. RIF + dapsone only slightly better (82% improved) than placebo (75%) in small study *(IJID 6 60, 2002)*
O. Mycobacterium xenopi	Regimen(s) not defined *(CID 24 226 & 233, 1997)*. Some recommend a **macrolide** + (**RIF** or **rifabutin**) + **ETB** ± **SM** *(AJRCCM 156 S1, 1997)* or **RIF** + **INH** ± **ETB** *(Resp Med 97 439, 2003)* but recent study suggests no need to treat in most pts with HIV *(CID 37 1250, 2003)*		In vitro: sensitive to clarithro *(AAC 36 2841, 1992)* and rifabutin *(JAC 39 567, 1997)* and many standard antimycobacterial drugs. Clarithro-containing regimens more effective than RIF/INH/ETB regimens in mice *(AAC 45 3229, 2001)*. FQs, linezolid also active in vitro
Mycobacterium lepraa (leprosy) Paucibacillary (tuberculoid or indeterminate) Multibacillary (lepromatous or borderline) ***See Comment for erythema nodosum leprosum*** Rev *Lancet 363 1209, 2004*	**Dapsone** 100 mg daily, unsupervised + **RIF** 600 mg po 1x/month, supervised for 6 months		Side-effects overall 0.4%. Single lesion paucibacillary disease may be treated with single-dose rx (RIF 600 mg + oflox 400 mg + minocycline 100 mg) *(Ln 353 655, 1999)*
	[**Dapsone** 100 mg daily + **CLO** 50 mg daily, unsupervised] + [**RIF** 600 mg + **CLO** 300 mg, 1x/month, supervised] for 24 months *(WHO Tech Rpt 874 1, 1998)*. Recent data suggest 12 mos rx effective *(Ln 353 655, 1999)*	**Ethionamide** (250 mg daily) or **prothionamide** (375 mg daily) may be substituted for CLO	Side-effects overall 5.1%. For erythema nodosum leprosum: prednisone 60–80 mg/d or thalidomide 300 mg/d *(BMJ 44 775, 1988; AJM 108 487, 2000)*. CLO available from Ciba-Geigy [(908) 277-3572]. Pefloxacin 800 mg qd po, oflox 400 mg qd po, sparfloxacin 200 mg qd po bactericidal and effective clinically with 4 log ↓ in organisms in small trials *(Int J Leprosy 58 281, 1990; AAC 38 662, 1994; AAC 38 61, 1994)*. Clarithro also rapidly bactericidal *(AAC 38 515, 1994)*. (Good reference: *Ln 345 4, 1995*.) 1 recent study suggests dapsone monotherapy as effective as combination rx for multibacillary leprosy *(AAC 38 2249, 1994)*. Regimens incorporating clarithro, minocycline, RIF, moxifloxacin, and/or oflox also show promise *(AAC 41 1618, 1997; AAC 44 2919, 2000)*. High relapse rate in pts treated with daily RIF + oflox for 4 wks *(AAC 41 1953, 1997)*. Resistance to dapsone: RIF & oflox reported *(Ln 349 103, 1997)*. Dapsone (or acedapsone[NUS]) effective for prophylaxis *(J Inf 41 137, 2000)*

* *Dosages are for adults (unless otherwise indicated) and assume normal renal function*

† **DOT** = directly observed therapy

TABLE 12A (8)

Abbreviations: **AMK** = amikacin **ATS** = American Thoracic Society **Azithro** = azithromycin, **BL/BLI** = β-lactam/β-lactamase inhibitors, **CIP** = ciprofloxacin **Clarithro** = clarithromycin **CLO** = clofazimine **CXR** = chest x-ray **dc** = discontinue **ddC** = zalcitabine **DOT** = directly observed therapy **ETB** = ethambutol **FQ** = fluoroquinolones **IA** = injectable agent (may include aminoglycosides (streptomycin amikacin or kanamycin) or the polypeptide capreomycin **IDSA** = Infectious Diseases Society of America **IMP** = imipenem cilastatin **INH** = isoniazid **INH-CR** = complete INH resistance **KM** kanamycin **Neomacrolides** = azithromycin clarithromycin roxithromycin **NUS** = not available in the U S **Oflox** = ofloxacin **pts** = patients **PZA** = pyrazinamide **RFB** = rifabutin **RFP** = rifapentine **RIF** = rifampin **rx** = treatment, **sens** = sensitive **SM** = streptomycin **TBc** = tuberculosis, **TMP/SMX** = trimethoprim/ sulfamethoxazole

TABLE 12B: DOSAGE, PRICE AND SELECTED ADVERSE EFFECTS OF ANTIMYCOBACTERIAL DRUGS[1]

AGENT (TRADE NAME)	USUAL DOSAGE	ROUTE/1° DRUG RESISTANCE (RES) US[1]/COST*	SIDE-EFFECTS, TOXICITY AND PRECAUTIONS	SURVEILLANCE
FIRST LINE DRUGS				
Ethambutol (Myambutol)	25 mg/kg/day for 2 months & then 15 mg/kg/d qd as 1 dose (<10% protein binding) [Bactenostatic to both extracellular & intracellular organisms]	po RES [2] 0 3% (0–0 7%) 400 mg tab $2 00	**Optic neuritis** with decreased visual acuity central scotomata, and loss of green and red perception peripheral neuropathy and headache (~1%) rashes (rare) arthralgia (rare), hyperuricemia (rare) Anaphylactoid reaction (rare) *Comment* Primarily used to inhibit resistance Disrupts outer cell membrane in M avium with ↑ activity to other drugs	Monthly visual acuity & red/green with dose >15 mg/kg/day ≥10% loss considered significant Usually reversible if drug discontinued
Isoniazid (INH) (Nydrazid Laniazid Teebaconin)	Daily dose 5–10 mg/kg/day up to 300 mg/day as 1 dose Twice weekly dose 15 mg/kg (900 mg maximum dose) (< 10% protein binding) [Bactericidal to both extracellular and intracellular organisms] Add pyridoxine in alcoholic pregnant or malnourished pts	po RES 4 1% (2 6–8 5%) 300 mg tab $0 02 IM (IV route not FDA-approved but has been used, esp in AIDS) 100 mg/ml in 10 ml vials (IM) $16 64	Overall ~1% Liver **Hepatitis** (children 10% mild ↑ SGOT normalizes with continued rx age <20 yrs rare 20–34 yrs 1 2% ≥50 yrs 2 3%) [also ↑ with daily alcohol & previous exposure to hepatitis C (usually asymptomatic—*CID 36 293, 2003*)] May be fatal With prodromal sx dark urine do LFTs discontinue if SGOT >3–5x normal **Peripheral neuropathy** (17% on 6 mg/kg/d less on 300 mg incidence ↑ in slow acetylators) **pyridoxine 10 mg daily will ↓ incidence** other neurologic sequelae, convulsions, optic neuritis toxic encephalopathy, psychosis muscle twitching dizziness coma (all rare) allergic skin rashes fever minor disulfiram-like reaction flushing after Swiss cheese, blood dyscrasias (rare) + antinuclear (20%) **Drug-drug interactions** common, *see Table 22*	Pre-rx liver functions Repeat if symptoms (fatigue weakness malaise anorexia nausea or vomiting) >3 days *(AJRCCM 152 1705 1995)* Some recommend SGOT at 2 4 6 months esp if age >50 years Clinical evaluation every month
Pyrazinamide	25 mg/kg/day (maximum 2 5 gm/d) qd as 1 dose [Bactericidal for intracellular organisms]	po 500 mg tab $1 04	**Arthralgia; hyperuricemia** (with or without symptoms) hepatitis (not over 2% if recommended dose not exceeded) gastric irritation, photosensitivity (rare)	Pre-rx liver functions Monthly SGOT uric acid Measure serum uric acid if symptomatic gouty attack occurs
Rifamate®—combination tablet	2 tablets single dose qd	po (1 hr before meal) 1 tab $2 58	1 tablet contains 150 mg INH 300 mg RIF	As with individual drugs
Rifampin (Rifadin Rimactane Rifocin)	10 0 mg/kg/day up to 600 mg/day qd as 1 dose (60–90% protein binding) [Bactericidal to all populations of organisms]	po RES 0 2% (0–0 3%) 300 mg cap $1 90 (IV available, Merrell-Dow Cost 600 mg $90 28)	INH/RIF dc'd in ~3% for toxicity gastrointestinal irritation antibiotic-associated colitis, drug fever (1%) pruritus with or without skin rash (1%) anaphylactoid reactions in HIV+ pts mental confusion thrombocytopenia (1%) leukopenia (1%) hemolytic anemia, transient **abnormalities in liver function "Flu syndrome"** (fever chills headache bone pain shortness of breath) seen if RIF taken irregularly or if daily dose restarted after an interval of no rx **Discolors urine, tears, sweat, contact lens en orange-brownish color.** May cause drug-induced lupus erythematosus *(Ln 349 1521, 1977)*	Pre-rx liver function Repeat if symptoms **Multiple significant drug-drug interactions, see Table 22**
Rifater®—combination tablet *(See Side-Effects)*	Wt ≥55 kg, 6 tablets single dose qd	po (1 hr before meal) 1 tab $1 91	1 tablet contains 50 mg INH 120 mg RIF, 300 mg PZA Used in 1st 2 months of rx (PZA 25 mg/kg) Purpose is convenience in dosing, ↑ compliance *(AnIM 122 951, 1995)* but cost 1 58 more Side-effects = individual drugs	As with individual drugs PZA 25 mg/kg
Streptomycin	15 mg/kg IM qd 0 75–1 0 gm/day initially for 60–90 days then 1 0 gm 2–3 times/week (15 mg/kg/day) qd as 1 dose	IM (or IV) RES 3 9% (2 7–7 6%) 1 0 gm $6 45	Overall 8% **Ototoxicity** vestibular dysfunction (vertigo) paresthesias dizziness & nausea (all less in pts receiving 2–3 doses/week) tinnitus and high frequency loss (1%) nephrotoxicity (rare), peripheral neuropathy (rare) allergic skin rashes (4–5%) drug fever Available from X-Gen Pharmaceuticals 607 732-4411 Ref re IV—*CID 19 1150, 1994* Toxicity similar with qd vs tid dosing *(CID 38 1538 2004)*	Monthly audiogram In older pts serum creatinine or BUN at start of rx and weekly if pt stable

[1] Note Malabsorption of antimycobacterial drugs may occur in patients with AIDS enteropathy For review of adverse effects, see *AJRCCM 167 1472 2003*

[2] **RES** = % resistance of M tuberculosis

See pages 90 & 92 for abbreviations page 88 for footnotes

* *Dosages are for adults (unless otherwise indicated) and assume normal renal function*

[1] **DOT** = directly observed therapy

TABLE 12B (2)

AGENT (TRADE NAME)	USUAL DOSAGE	ROUTE/1° DRUG RESISTANCE (RES) US[1]/COST**	SIDE-EFFECTS, TOXICITY AND PRECAUTIONS	SURVEILLANCE
SECOND LINE DRUGS (more difficult to use and/or less effective than first line drugs)				
Amikacin (Amikin)	7.5–10.0 mg/kg qd [Bactericidal for extracellular organisms]	IV or IM RES (est 0.1%) 500 mg NB $33, G $18.70	*See Table 10, pages 62 & 72* Toxicity similar with qd vs tid dosing *(CID 38:1538, 2004)*	Monthly audiogram. Serum creatinine or BUN weekly if pt stable
Capreomycin sulfate (Capastat sulfate)	1 gm/day (15 mg/kg/day) qd as 1 dose	IM or IV RES 0.1% (0–0.9%) 1 gm $26.90	Nephrotoxicity (36%) ototoxicity (auditory 11%) eosinophilia leukopenia skin rash fever hypokalemia neuromuscular blockade	Monthly audiogram biweekly serum creatinine or BUN
Ciprofloxacin (Cipro)	750 mg bid	po IV 750 mg (po) $4.80	TB not an FDA-approved indication for CIP. Desired CIP serum levels 4–6 µg/ml requires median dose 800 mg *(AJRCCM 151:2006, 1995)* Discontinuation rates 6–7% CIP well tolerated *(AJRCCM 151:2006, 1995)* FQ-resistant M. Tb identified in New York *(Ln 345:1148, 1995) See Table 10, pages 64 & 69 for adverse effects*	None
Clofazimine (Lamprene)	50 mg/d (unsupervised) + 300 mg 1x/month supervised or 100 mg/d	po (with meals) 50 mg $0.20	Skin **pigmentation (pink-brownish black)** 75–100% dryness 20% pruritus 5% GI abdominal pain 50% (rarely severe leading to exploratory laparoscopy) splenic infarction (VR), bowel obstruction (VR), GI bleeding (VR) Eye conjunctival irritation retinal crystal deposits	None
Cycloserine (Seromycin)	750–1000 mg/day (15 mg/kg/day) 2–4 doses/day [Bacteriostatic for both extracellular & intracellular organisms]	po RES 0.1% (0–0.3%) 250 mg cap $4.19	Convulsions **psychoses** (5–10% of those receiving 1.0 gm/day) headache somnolence hyperreflexia increased CSF protein and pressure **peripheral neuropathy** 100 mg pyridoxine (or more) daily should be given concomitantly Contraindicated in epileptics	None
Dapsone	100 mg/day	po 100 mg $0.20	Blood ↓ hemoglobin (1–2 gm) & ↑ retics (2–12%) in most pts Hemolysis in G6PD deficiency **Methemoglobinemia** CNS peripheral neuropathy (rare) GI nausea vomiting Renal albuminuria nephrotic syndrome Erythema nodosum leprosum in pts rx for leprosy (½ pts 1st year)	None
Ethionamide (Trecator-SC)	500–1000 mg/day (10–15 mg/kg/d) 1–3 doses/day [Bacteriostatic for extracellular organisms only]	po RES 0.8% (0–1.5%) 250 mg tab $3.09	**Gastrointestinal irritation** (up to 50% on large dose) goiter peripheral neuropathy (rare) convulsions (rare) changes in affect (rare) difficulty in diabetes control rashes hepatitis purpura stomatitis gynecomastia menstrual irregularity Give drug with meals or antacids 50–100 mg pyridoxine per day concomitantly SGOT monthly Possibly teratogenic	
Ofloxacin (Floxin)	400 mg bid	po IV 400 mg (po) $6.67	Not FDA aporoved indication Overall adverse effects 11% 4% discontinued due to side-effects GI nausea 3% diarrhea 1% **CNS** insomnia 3%, headache 1% dizziness 1%	
Para-aminosalicylic acid (PAS Paser) (Na^+ or K^+ salt)	4–6 gm bid (200 mg/kg/day) [Bacteriostatic for extracellular organisms only]	po RES 0.8% (0–1.5%) 450 mg tab $0.08 *(see Comment)*	**Gastrointeetinal irritation** (10–15%) goitrogenic action (rare), depressed prothrombin activity (rare) G6PD mediated hemolytic anemia (rare) drug fever rashes hepatitis myalgia arthralgia Retards hepatic enzyme induction may ↓ INH hepatotoxicity Available from CDC (404) 639-3670 Jacobus Pharm. Co. (609) 921-7447	None
Rifabutin (Mycobutin)	300 mg/day (prophylaxis or treatment)	po 150 mg $6.84	Polymyalgia polyarthralgia leukopenia granulocytopenia Anterior uveitis when given with concomitant clarithromycin avoid 600 mg dose *(NEJM 330:438, 1994)* Uveitis reported with 300 mg/d *(AnIM 12:510, 1994)* Reddish urine orange skin (pseudojaundice)	None
Rifapentine (Priftin)	600 mg twice weekly for 1st 2 mos then 600 mg q week	po 150 mg $3.00	Similar to other rifabutins *(See RIF, RFB)* Hyperuricemia seen in 21% Causes red-orange discoloration of body fluids Note ↑ prevalence of RIF resistance in pts on weekly rx *(Ln 353:1843, 1999)*	None
Thalidomide (Thalomid)	100–300 mg po qd (may use up to 400 mg po qd for severe erythema nodosum leprosum)	po 50 mg $27.90	**Contraindicated in pregnancy. Causes severa life-threatening birth defects. Both male and female patients must use barrier contraceptive methods (Pregnancy Catagory X). Frequantly causes drowsineaa or somnolance. May causa peripheral neuropathy.** *(AJM 108:487, 2000)* For review *see Lancet 363:1803, 2004*	Available only through pharmacists participating in System for Thalidomide Education and Prescribing Safety (S.T.E.P.S.)

* Adult dosage only. [1]Mean (range) (higher in Hispanics, Asians, and patients < 10 years old). ** Average wholesale price according to 2004 DRUG TOPICS RED BOOK, Medical Economics.
Abbreviations. **VR** = very rare **aap** = especially **dc** = discontinue **RES** = % resistance to M. tuberculosis

See pages 90 & 92 for abbreviations, page 88 for footnotes. * *Dosages are for adults (unless otherwise indicated) and assume normal renal function.* [1] **DOT** = directly observed therapy

TABLE 13A: TREATMENT OF PARASITIC INFECTIONS

Many of the drugs suggested are not licensed in the United States. The following are helpful resources available through the Center for Disease Control and Prevention (CDC) in Atlanta. Website is www.cdc.gov. General advice for parasitic diseases other than malaria: (770) 488-7760 or (770) 488-7775.
For CDC Drug Service[1]: 8:00 a.m. – 4:30 p.m. EST (404) 639-3670 (or -2888); emergency after hours: (404) 639-2888; fax: (404) 639-3717.
For malaria: Prophylaxis advice (770) 488-7788 or (877) 394-3228 or (877) 394-8747; treatment (770) 488-7788; website: www.cdc.gov/travel; fax (888) 232-3299.
NOTE: All dosage regimens are for adults with normal renal function unless otherwise stated.
For licensed drugs: suggest checking package inserts to verify dosage and side-effects. Occasionally, post-licensure data may alter dosage as compared to package inserts.
For abbreviations of journal titles: *see Table 1, page 45* **Reference with pediatric dosages: *Medical Letter on-line version: www.medletter.com (August 2004)***

INFECTING ORGANISM	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
PROTOZOA—INTESTINAL (non-pathogenic: E. hartmanni, E. dispar, E. coli, Iodamoeba butschlii, Endolimax nana, Chilomastix mesnili)			
Balantidium coli	**Tetracycline** 500 mg po qid x10 d	**Metronidazole** 750 mg po tid x5 d	*See Table 10B for side-effects*
Blastocystis hominis	Role as pathogen supported: random trial metro vs placebo	**Metronidazole** 750 mg po tid x10 d. **High dose** increases risk of adverse effects. **Alternatives: Iodoquinol** 650 mg po tid x20 d, or TMP/SMX-DS, one bid x7 d	
Cryptosporidium parvum and hominis Treatment is unsatisfactory Ref: *CID 39:504, 2004*	**Immunocompetent—No HIV:** **Nitazoxanide** 500 mg po bid x3 d	**HIV with immunodeficiency:** **Nitazoxanide** 500 mg po bid x14 d: in adults (60% response). No response in HIV+ children	**Nitazoxanide:** Approved in liquid formulation for rx of children & 500 mg tabs for adults. Ref: *Med Lett 45:29, 2003*. C. hominis assoc. with ↑ in post-infection eye & joint pain, recurrent headache, & dizzy spells *(CID 39:504, 2004)*
Cyclospora cayetanensis	Immunocompetent pts: **TMP/SMX-DS** tab 1 po bid x7–10 d	AIDS pts: **TMP/SMX-DS** tab 1 po qid x10 d, then tab 1 po 3x/week	Ref: *CID 23:429, 1996*. If sulfa-allergic: **CIP** 500 mg po bid x7 d, & then 1 tab po 3x/wk x2 wks
Dientamoeba fragilis	**Iodoquinol** 650 mg po tid x20 d	**Tetracycline** 500 mg po qid x10 d, OR **Metronidazole** 500–750 mg po tid x10 d	Other alternatives: doxy 100 mg po bid x10 d, paromomycin 500 mg po tid x7 d
Entamoeba histolytica; ameblasis Reviews: *Ln 361:1025, 2003; NEJM 348:1563, 2003*			
Asymptomatic cyst passer	**Paromomycin** (aminosidine in U.K.) 500 mg po tid x7 d, OR **Iodoquinol** 650 mg po tid x20 d	**Diloxanide furoate**[NUS] (Furamide) 500 mg po tid x10 d. (Source: Panorama Compound Pharm. 800-247-9767)	Metronidazole not effective vs cysts
Patient with diarrhea/dysentery, mild/moderate disease. Oral rx possible	**Metronidazole** 500–750 mg po tid x10 d, or **tinidazole** 2 gm once daily x3 d, followed by	(**Tinidazole** 1.0 gm po q12h x3 d.) or (**ornidazole**[NUS] 500 mg po q12h x5 d.), followed by	Drug side-effects in Table 10B Colitis can mimic ulcerative colitis; ameboma can mimic adenocarcinoma of colon
	Either [**paromomycin** 500 mg po tid x7 d.] or [**Iodoquinol** (was diiodohydroxyquin) 650 mg po tid x20 d.]		**Dx:** antigen detection & PCR better than O&P *(Clin Micro Rev 16:713, 2003)*. Watch out for non-pathogenic E. dispar *(Ln 351:1672, 1998)*
Severe or extraintestinal infection, e.g. hepatic abscess	(**Metronidazole** 750 mg **iV to PO** tid x10 d, or **tinidazole** 2 gm once daily x5 d.) followed by **paromomycin** 500 mg po tid x7 d		**Serology positive (antibody present) with extraintestinal disease.**
Giardia lamblia; giardiasis	(**Tinidazole** 2.0 gm po x1) OR (**nitazoxanide** 500 mg po bid x3 d.)	**Metronidazole** 500–750 mg po tid x5 d (high frequency of GI side-effects). *See Comment* Rx if pregnant: **Paromomycin** 500 mg 4x/d x7 d	**Refractory pts: (metro 750 mg po + quinecrine[2] 100 mg po)** —both 3x/d x3 wks. Ref: *CID 33:22, 2001* **Nitazoxanide** ref: *CID 32:1792, 2001*
Isospora belli	**TMP/SMX-DS** tab 1 po bid x10 d; if AIDS pt: TMP/SMX-DS qid x10 d & then bid x3 wks	(**Pyrimathamine** 75 mg/d po + **folinic acid** 10 mg/d po) x14 d. **CIP** 500 mg po bid x7 d — 87% response *(AnIM 132:885, 2000)*	Chronic suppression in AIDS pts: either 1 TMP/SMX-DS tab 3x/wk OR (pyrimethamine 25 mg/d po + folinic acid 5 mg/d po)

[1] **Druga available from CDC Drug Service: 404-639-2888 or –3670 or www.cdc.gov/ncidod/arp/druge/formulery.html: Bithionol, dahydroemetine, diethyicerbamazine (DEC), melersoproi, nifurtimox, etibogiuconate (Pentostam), euramin.**
[2] Quinacrine available from Panorama Compounding Pharmacy (800) 247-9767 (818) 988-7979

* *All doses are for adults(unless otherwise indicated) and assume normal renal function. See page 103 for abbreviations*

TABLE 13A (2)

INFECTING ORGANISM	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
PROTOZOA—INTESTINAL *(continued)*			
Microsporidiosis *(Ref CID 27 1, 1998)*			
Ocular Encephalitozoon hellum or cuniculi Vittaforma corneae (Nosema sp.)	**Albandazole** 400 mg po bid x3 weeks	In HIV+ pts, reports of response of E hellum to **fumagillin** eyedrops *(see Comment)* For V corneae may need keratoplasty	To obtain fumagillin 800-292 6773 or www letterrx com Neutropenia & thrombocytopenia serious adverse events Dx Most labs use modified trichrome stain Need electron micrographs for species identification FA and PCR methods in development
intestinal (diarrhea) Enterocytozoon bieneusi Encephalitozoon (Septata) intestinalis	**Albendazole** 400 mg po bid x3 weeks	Oral **fumagillin 20 mg po tid** reported effective for E bieneusi *(NEJM 346 1963, 2002)—see Comment*	
Disseminated E hellum cuniculi or intestinalis Pleistophora sp , *others in Comment*	**Albendazole** 400 mg po bid x3 weeks	No established rx for Pleistophora sp	For Trachipleistophora sp , try itraconazole + albendazole *(NEJM 351 42, 2004)* Other pathogens Brachiola vesicularum & algerae *(NEJM 351 42, 2004)*
PROTOZOA—EXTRAINTESTINAL			
Amabic maningoencaphalitis			
Acanthamoeba sp — no proven rx Rev *Clin Micro Rev 16 273 2003*	Success with IV **pentamidina** topical **chlorhaxidina** & 2% **katoconazola** cream & then po **itra** *(NEJM 331 85 1994)* 2 children responded to po rx **TMP/SMX** + **rifampin**+ **kato** *(PIDJ 20 623, 2001)*		For treatment of keratitis, *see Table 1, page 9*
Balamuthia mandrillaris	**Pantamidina** + **clarithro** + **flucon** + **sulfadiazina** + **flucytosina** *(CID 37 1304, 2003, Arch Path Lab Med 128 466, 2004)* A cause of chronic granulomatous meningitis		
Naegleria fowleri >95% mortality	**Ampho B** 1 5 mg/kg/d in 2 div doses & then 1 mg/kg/d IV x6 d		Case report Ampho, miconazole & RIF *(NEJM 306 346 1982)*
Sappinia diploidea	**Azithro** + **pantamidina** + **itra** + **flucytosina** *(JAMA 285 2450, 2001)*		
Babesia microti; babesiosis *(CID 22 1117, 2001)*	**Atovaquona** 750 mg bid po x7–10 d + **azithro** 600 mg po daily x7–10 d *(NEJM 343 1454, 2000)*	(**Clindamycin** 600 mg po tid) + (**quinina** 650 mg po tid) x7–10 d For adults can give **clinda** IV as 1 2 gm bid	Can cause overwhelming infection in asplenic patients Reported in Washington State *(EIN 10 622, 2004)*
Ehrlichiosis—*See Table 1 page 39*			
Leishmaniasis NOTE: Responses of various species differ—see *reference*			
Visceral—Kala-azar L donovani India/Africa L infantum Mediterranean L chagasi New World **WARNING: Avoid combined antimony & ampho B** *(Ln 351 1928 1998)*	**Miltefosina**[NUS] drug of choice—*see Comment* **Adults:** 2 5 mg/kg/d po either as once or twice daily x28 d **Children** (<12 yrs old) 2 5 mg/kg/d in 3 div doses after meals x28 d Refs *NEJM 347 1737, 1739, & 1794, 2002, PIDJ 22 434, 2003*	**Lipid formulations of ampho B** effective in short-course regimens but impractical due to expense **Children** Liposomal ampho B → 98% success *(CID 36 560, 2003)* in dose of 10 mg/kg/d x2 days **Adults** Liposomal Ampho B 2 mg/kg/d x5 d *(CID 38 377, 2004)*	Antimony resistance a problem in India *(JID 180 564 1999)* **Antimony** (**atibogluconate** or **magiumina antimonata**) 20 mg/kg/d of antimony (Sb) (in 2 div doses) IM or IV x28 d Not marketed in U S Contact CDC Drug Service (404) 639-3670 **Miltefosina:** Available from Zentaris, Frankfurt Germany Impavido@zentaris de
Mucosal—L. braziliensis	**Antimony** as for Visceral	**Ampho B**[1] 1 mg/kg IV qod x20–30 doses	Approx cure rates antimony 60%, AmB >75%
Cutaneous: ***Most resolve spontaneously; Rx goal: ↓ time to cure & prevention of mucocutaneous spread*** New World Multiple species Old World L tropica & L major	**Fluconazola** 200 mg po once daily x6 wks Effective vs L major *(NEJM 346 891, 2002)* New World vs L v panamensis **Miltefosine**[NUS] 2 5 mg/kg po 1x/d x28 d 91% success *(CID 38 1266, 2004)*	Other options all IV **Antimony** as for visceral or **Pentamidina** 2–4 mg/kg qd or q2 days IV x15 doses	For miltefosine contact Zentaris impavido@zentaris de Treatment is species-specific Good review (does not include miltefosine) *JAC 53 158 2004*

TABLE 13A (3)

INFECTING ORGANISM	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
PROTOZOA—EXTRAINTESTINAL *(continued)*			
Malaria (Plasmodia species)—NOTE: CDC Malaria info—prophylaxis (877) 394-8747; treatment (770) 488-7788. Websites: www.cdc.gov/ncidod/dpd/parasites/malaria/default.htm, www.who.int/health-topics/malaria.htm.			
Prophylaxis—Drugs plus personal protection screens nets 30–35% DEET skin repellent (avoid 95% products in children) permethrin spray on clothing and nets *(Ann IM 128 931 1998)*			
For areas **free** of chloroquine (CQ) resistant P. falciparum Haiti Dominican Republic Central America west and north of the Panama Canal and parts of the Middle East	**CQ**[1] 500 mg (300 mg base) po per week starting 1–2 wks before travel during travel & 4 wks post travel **or AP**[1] 1 adult tab/day	**CQ Peds dose:** 8 3 mg/kg (5 mg/kg of base) po 1x/wk up to 300 mg (base) max dose **or AP** by weight (peds tabs) 11–20 kg 1 tab 21–30 kg 2 tabs 31–40 kg 3 tabs >40 kg 1 adult tab/day	CQ safe during pregnancy **The areas free of CQ-resistant falciparum malaria continue to shrink:** Central America north of Panama Canal Haiti and parts of Middle East CQ-resistant falciparum malaria reported from Saudi Arabia Yemen Oman & Iran
For areas with **CQ-resistant P. falciparum** CDC voice info on prophylaxis at (888) 232-3228 or website www cdc gov Ref *JAMA 278 1767 1997*	**Atovaquone** 250 mg—**proguanil** 100 mg (**Malarone**) comb tablet 1/day with food 1–2 d prior to during & 7 d post-travel Peds dose in footnote[2] Cost/2 wks $125	**Doxycycline** 100 mg po daily for adults & children >12 years of age[2] Cost/2 wks $30 **OR Mefloquine (MQ)**[1] 250 mg (228 mg base) po per week 1 wk before during and for 4 wks after travel Cost/2 wks $80 Peds dose in footnote[2]	**Pregnancy: MQ current best option** Insufficient data with **Malarone Avoid doxycycline and primaquine. Primaquine** Used only if prolonged exposure to endemic area (e g Peace Corps) **Can cause hemolytic anemia if G6PD deficiency present. MQ not recommended** if cardiac conduction abnormalities seizures or psychiatric disorders e g , depression psychosis MQ outside U S 275 mg tab contains 250 mg of base Malarone resistance *CID 37 450, 2003*
	Another option for adults **primaquine (PQ)** 30 mg base po daily in non-pregnant G6PD-neg travelers 88% protective vs P falciparum & >92% vs P vivax *(CID 33 1990 2001)*		
Treatment *(NEJM 335:800, 1996)* (P. falciparum, P. vivax, P. malariae, P. ovale) Blood smear consistent with **P. vivax &/or P. ovale** CDC Malaria treatment— (770) 488-7788 or website www cdc gov	**For chloroquina (CQ)-sensitive plasmodia: CQ** [1 0 gm (=600 mg base) po 0 5 gm in 6 hrs, then 0 5 gm daily x2 d] + **Primequine (PQ)** 26 3 mg (15 mg base) po daily x14 d Check for severe G6PD deficiency before rx *(CID 39 1336 2004)*	**CQ-resistant P. vivax** *(see Comment)* [**Quinina sulfate (QS)** 650 mg po q8h x3–7 d + **doxycycline** 100 mg bid x7 d] OR **mefloquina** 750 mg po then 500 mg 12 hrs later OR **halofantrine** 500 mg po q6h x3 doses To prevent relapses give PQ 26 3 mg (15 mg base) 1 tab po daily x14 d screen for G6PD def to avoid severe hemolysis	**CQ-resistant P. vivax reported from Oceania and South America** Rx as CQ resistant P falciparum **Pregnancy** CQ safe all trimesters No PQ in pregnancy or to newborns—risk of hemolysis Peds rx doses For **CQ** 10 mg of **base** per kg po then 5 mg base/kg at 12 24 36 hrs For **PQ** use 0 3 mg **base**/kg/d x14 d
Blood smear consistent with P. falciparum or P. malariae: CQ-sensitive	**Chloroquina (CQ)** as for CQ sensitive P vivax Don t need **primaquine (PQ).** CQ-resistant P falciparum *see below*	Assumes P falciparum CQ sensitive i e acquired in Central America (west of Panama Canal), Haiti and most of Middle East	
Blood smear shows P. falciparum assumed CQ-resistant PQ therapy possible. Ref *NEJM 335 800, 1996* Rx same for CQ-resistant P vivax	[**Quinine sulfate (QS)** 325 mg (=250 mg base) Give 650 mg po 3x/d] + (**doxycycline** 100 mg po bid)— both x7 d **Peds QS** x3 d + **Fansidar** x1 dose on last day of QS *(dosage in footnote[3])* or **Atovaquone/proguanil 1 gm/400 mg (4 adult tabs) po 1x/day for 3 days** with food Peds dose in footnote[3]	Areas of drug resistance, e g NW Thailand (**Artesunate**[NUS] 4 mg/kg/d po x3 d + **mefloquine** 750 mg po & then 500 mg 12 hrs later) Artesunate ref *AAC 47 901, 2003*	**Other rx alternatives:** (1) **MQ**[1] 750 mg then 500 mg 12 hrs later (peds & adults) Resistance reported *(JID 180 2077 1999)* (2) **Halofantrine** 500 mg po q6h x3 doses Repeat regimen in 1 wk **Pregnancy** High morbidity/mortality Despite concerns of potential fetal toxicity use **quinine** or **IV quinidine** followed by **Fansidar** (sulfadoxine-pyrimethamine) 3 tablets (each tab 25/500 mg) or 1500 mg **sulfadoxine** + 75 mg **pyrimethamine** x1 dose Alternatives [Quinine + doxycycline (despite fetal concerns)] OR [quinine + clindamycin *(AAC 46 2315, 2002)*] **Do not use AP during pregnancy.**

[1] **AP** = atovaquone proguanil **CQ** = chloroquine phosphate **MQ** = mefloquine **PQ** = primaquine **QS** = quinine sulfate

[2] **Peds prophylaxis dosages** (Ref *CID 34 493, 2002*)**: Mefloquine** weekly dose by **weight** in kg <15 = 5 mg/kg 15–19 ¼ adult dose 20–30 = ½ adult dose 31–45 = ¾ adult dose >45 = adult dose **Atovaquone/proguanil** by **weight** in kg, single daily dose 11–20 kg 62 5/25 mg 21–30 kg 125/50 mg, 31–40 kg 187 5/75 mg >40 kg 250/100 mg **Doxycycline** ages >8–12 yrs 2 mg/kg/d up to 100 mg/day

[3] **Pediatric treatment dosage** (Ref *CID 37 1340, 2003*)**: QS** 25 mg/kg/d (max 2 gm/d) po div q8h x3 d + a single po dose of **Fanaidar** (pyrimethamine sulfadoxine) given on last day of quinine Fansidar single dose by age (yr) of pt <1 = ¼ tab 1–3 = ½ tab 4–8 yrs = 1 tab 9–14 = 2 tabs >14 = 3 tabs **Atovaquone/proguanil** single daily dose by weight 5–8 kg 125/50 mg 9–10 kg 187 5/75 mg 11–20 kg, 250/100 mg 21–30 kg 500/200 mg, 31–40 kg 750/300 mg >40 kg, 1 gm/400 mg all x3 days **Mefloquine** <45 kg, 15 mg/kg then 10 mg/kg 12 hrs later **Halofantrine** <40 kg 8 mg/kg q6h x3 repeat in 1 week

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function *See page 103 for abbreviations*

TABLE 13A (4)

INFECTING ORGANISM	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
PROTOZOA—EXTRAINTESTINAL/Malaria/Treatment *(continued)*			
Blood smear consistent with **P. falciparum** **Pt too ill for initial po therapy** **NOTE:** Steroids are harmful in cerebral malaria Drug resistance ref *Ln Inf Dis 2 209 2002*	In U S **Quinidine gluconate** in normal saline [10 mg/kg IV over 1 hr then 0 02 mg/kg/min (monitor EKG) x72 hrs)] OR [15 mg/kg IV over 4 hrs then 7 5 mg/kg IV over 4 hrs q8h x72 hrs] OR until patient can take po meds **NOTE:** No loading dose if mefloquine or quinine in past 24 hrs	Outside U S **Quinine dihydrochloride**[NUS] in 5% dextrose 20 mg/kg IV over 4 hrs then 10 mg/kg over 2–8 hrs q8h x72 hrs OR **Artemether**[NUS] 3 2 mg/kg IM then 1 6 mg/kg IM daily For both switch to po regimen when possible to finish 7 days of rx	May be manifest as cerebral malaria, renal failure or ARDS **Monitor parasitemia!** If rx effective expect ≥75% ↓ parasite count after 48 hrs of rx If parasitemia exceeds 15% consider **exchange transfusion** efficacy unclear *(CID 34 1192, 2002)* CDC Malaria info (770) 488-7788 **Pregnancy** *See Comment, po therapy, bottom of page 95*
Malaria—self initiated treatment Only for emergency situation where medical care not available	**Atovaquone-proguanil** 4 adult tabs (1 gm/400 mg) po daily x3 d	**Fansidar** (25 mg pyrimethamine + 500 mg sulfadoxine) 3 tabs po x1 dose	
Microsporidia—systemic *—see page 94, Intestinal Protozoa*			
Pneumocystis carinii Pneumonia (PCP). New name is **Pneumocystis jiroveci** (yee-row-vek-ee) Mutations encoding resistance to sulfamethazole identified *(JID 188 1017 2003)*			
Not acutely ill, able to take po meds PaO_2 >70 mmHg	(**TMP/SMX-DS** 2 tabs po q8h x21 d) OR (**Dapsone** 100 mg po qd + **trimethoprim** 5 mg/kg po tid x21 d)	[**Clindamycin** 300–450 mg po q6h + **primaquine** 15 mg base po qd] x21 d OR **Atovaquone** suspension 750 mg po bid with food x21 d	DAP/TMP TMP/SMX clinda/prima regimens equally effective Rash/fever 10% with DAP/TMP 19% with TMP/SMX 21% with clinda/prima Ref clinda/prim vs TMP/SMX *CID 27 524 1998* Dapsone ref *CID 27 191 1998* **After 21 days, chronic suppression in AIDS pts** ***(see below).***
	NOTE Concomitant use of corticosteroids usually reserved for sicker pts with PaO_2 <70 *(see below)*		
Acutely ill, po rx not possible PaO_2 <70 mmHg	[**Prednisone** (15–30 min before TMP/SMX) 40 mg po bid x5 d then 40 mg qd x5 d then 20 mg po qd x11 d] + [**TMP/SMX** (15 mg of TMP component/kg/ d) IV div q6–8h x21 d]	**Prednisone** as in primary rx PLUS [(**Clinda** 600 mg IV q8h) + (**primaquine** 30 mg base po qd)] x21 d OR **Pentamidine** 4 mg/kg/d IV x21 d	**After 21 days, chronic suppression in AIDS pts** ***(see below).*** **PCP can occur in absence of HIV infection and steroids** ***(CID 25:215 & 219, 1997).***
	Can substitute IV prednisolone (reduce dose 25%) for po prednisone		
Primary prophylaxis and post-treatment suppression Refs *MMWR 51(RR-8) 6/14/2002 AnIM 137 435 2002*	(**TMP/SMX-DS or -SS** 1 tab po qd or 1 DS 3x/wk) OR (**dapsone** 100 mg po qd) DC when CD4 >200 x3 mos *(NEJM 344 159 2001)*	[(**Pentamidine** 300 mg in 6 ml sterile water by aerosol q4 wks) OR (**dapsone** 200 mg po + **pyrimethamine** 75 mg po + **folinic acid** 25 mg po—**all once a week**) or **atovaquone** 1500 mg po qd with food	TMP/SMX-DS regimen provides cross-protection vs toxo and other bacterial infections Dapsone + pyrimethamine protects vs toxo Atovaquone suspension 1500 mg once daily as effective as daily dapsone *(NEJM 339 1889 1998)* & inhaled pentamidine *(JID 180 369 1999)*
Toxoplasma gondii (Reference *Ln 363 1965 2004)* **Immunologically normal patients** *(For pediatric doses, see reference)*			
Acute illness with lymphadenopathy	No specific rx unless severe/persistent symptoms or evidence of vital organ damage		
Acquired via transfusion (lab accident)	Treat as for active chorioretinitis		
Active chorioretinitis meningitis lowered resistance due to steroids or cytotoxic drugs	[**Pyrimethamine** (pyri) 200 mg po once on 1st day then 50–75 mg qd] + [**sulfadiazine** *(see footnote[1])* 1–1 5 gm po qid] + [**leucovorin (folinic acid)** 5–20 mg 3x/week]—**see *Comment*.** Treat 1–2 wks beyond resolution of signs/symptoms continue leucovorin 1 wk after stopping pyri		For congenital toxo toxo meningitis in adults and chorioretinitis **add prednisone 1 mg/kg/d in 2 div. doses** until CSF protein conc falls or vision-threatening inflammation has subsided Adjust folinic acid dose by following CBC results
Acute in pregnant women	**Spiramycin** [From FDA call (301) 827-2335] 1 0 gm po q8h (without food) until term or until fetal infection NOTE Use caution in interpretation of commercial tests for toxoplasma IgM antibody for help FDA Advisory (301) 594 3060 or Toxoplasma Serology Lab of Palo Alto Med Found (650) 853-4828		IgG avidity test of help in 1st trimester *(J Clin Micro 42 941 2004)*
Fetal/congenital	Management complex Combination rx with pyrimethamine + sulfadiazine + leucovorin *see Comment*		Details in *Ln 363 1965 2004)* **Consultation advisable.**

[1] Sulfonamides for toxo Sulfadiazine now commercially available Sulfisoxazole much less effective

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function *See page 103 for abbreviations*

TABLE 13A (5)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
PROTOZOA—EXTRAINTESTINAL/Toxoplasma gondii *(continued)*			
Acquired immunodeficiency syndrome (AIDS)			
Cerebral toxoplasmosis Ref *Ln 363 1965 2004*	[**Pyrimethamine** (pyri) 200 mg x1 po then 75 mg/d po] + (**sulfadiazine** 1–1.5 gm po q6h) + (**folinic acid** 10–20 mg/d po) for 4–6 wks after resolution of signs/symptoms and then suppressive rx *(see below)* OR **TMP/SMX** 10/50 mg/kg/d po or IV div q12h x30 d *(AAC 42 1346 1998)*	[**Pyri** + **folinic acid** (as in primary regimen)] + 1 of the following (1) **Clinda** 600 mg po/IV q6h or (2) **clarithro** 1.0 gm po bid or (3) **azithro** 1.2–1.5 gm po qd or (4) **dapsone** 100 mg po qd or (5) **atovaquone** 750 mg po q6h Treat 4–6 wks after resolution of signs/symptoms then suppression	Use alternative regimen for pts with severe sulfa allergy If multiple ring-enhancing brain lesions (CT or MRI) >85% of pts respond to 7–10 days of empiric rx; if no response, suggest brain biopsy
Primary prophylaxis AIDS pts—IgG toxo antibody + CD4 count <100/µl	(**TMP/SMX-DS** 1 tab po qd) or (**TMP/SMX-SS** 1 tab po qd)	[(**Dapsone** 50 mg po qd) + (**pyri** 50 mg po q week) + (**folinic acid** 25 mg po q week)] OR **atovequone** 1500 mg po qd	Prophylaxis for pneumocystis also effective vs toxo Refs *MMWR 51(RR-8) 6/14/2002 AnIM 137 435 2002*
Suppression after rx of cerebral toxo	(**Sulfadiazine** 500–1000 mg po 4x/d) + (**pyri** 25–50 mg po qd) + (**folinic acid** 10–25 mg po qd) DC if CD4 count >200 x3 months	[(**Clinda** 300–450 mg po q6–8h) + (**pyri** 25–50 mg po qd) + (**folinic acid** 10–25 mg po qd)] OR **atovaquone** 750 mg po q6–12h	(Pyri + sulfa) prevents PCP and toxo (clinda + pyri prevents toxo only
Trichomonas vaginalis	*See Vaginitis, Table 1, page 17*		
Trypanosomiasis Ref *Ln 362 1469, 2003*			
West African sleeping sickness (T. brucei gambiense)			
Early: Blood/lymphatic—CNS OK	**Pentamidine** 4 mg/kg IM daily x10 d	(**Suramin** [COC]1 100 mg IV (test dose), then 1 gm IV on days 1, 3, 7, 14, & 21	
Late: Encephalitis	**Melarsoprol**[CDC1] 2.2 mg/kg/d IV x10 d	**Eflornithine** 100 mg/kg q6h IV x14 d	
Prophylaxis	**Pentamidine** 3 mg/kg IM q6 mos	Not for casual visitor	
East African sleeping sickness (T. brucei rhodesiense)			
Early: Blood/lymphatic	**Suramin**[COC1] 100 mg IV (test dose), then 1 gm IV on days 1, 3, 7, 14, & 21	None	
Late: Encephalitis	**Melarsoprol**[CDC1] 2–3.6 mg/kg/d IV x3 d, repeat after 7 d, & for 3rd time 7 d after 2nd course	Prednisone may prevent/attenuate encephalopathy	
T. cruzi—**Chagas disease** or acute American trypanosomiasis Ref *Ln 357 797 2001*	**Nifurtimox**[CDC1] 8–10 mg/kg/d po div 4x/d after meals x120 d. Ages 11–16 yrs: 12.5–15 mg/kg/d div qid po x90 d. Children <11 yrs: 15–20 mg/kg/d div qid po x90 d	**Benznidazole**[NUS] 5–7 mg/kg/d po div 2x/d x30–90 d *(AJTMH 63 111 2000)* NOTE: Avoid tetracycline and steroids	Treatment of no benefit in chronic late disease Nifurtimox reported 70–95% effective Immunosuppression for heart transplant can reactivate chronic Chagas disease
NEMATODES—INTESTINAL (Roundworms) For significance of eosinophilia see *CID 34 407 2002*			
Ascaris lumbricoides (**ascariasis**)	**Albendazole** 400 mg po x1 dose or **mebendazole** 100 mg po bid x3 d or 500 mg po x1 dose	**Ivermectin** 150–200 µg/kg po x1 dose or **nitazoxanide** 500 mg po bid x3 d	Can present with intestinal obstruction
Capillaria philippinensis (**capillariasis**)	**Mebendazole** 200 mg po bid x20 d	**Albendazole** 200 mg po bid x10 d	
Enterobius vermicularis (**pinworm**)	**Albendazole** 400 mg po x1, repeat in 2 wks OR **mebendazole** 100 mg po x1, repeat in 2 wks	**Pyrantel pamoate** 11 mg/kg (to max. dose of 1.0 gm) po x1 dose, repeat every 2 wks x2	*Side-effects in Table 13B, pages 101, 103*
Hookworm (Necator americanus and Ancylostoma duodenale)	**Albendazole** 400 mg po x1 or **mebendazole** 100 mg po bid x3 d	**Pyrantel pamoate** 11 mg/kg (to max. dose of 1.0 gm) po daily x3 d	NOTE: Ivermectin not effective. Eosinophilia may not be present but eggs detectable in stool

[1] **COC** = available from CDC Drug Service

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. See page 103 for abbreviations

TABLE 13A (6)

INFECTING ORGANISM	SUGGESTED REGIMENS		COMMENTS
	PRIMARY	ALTERNATIVE	
NEMATODES—INTESTINAL (Roundworms) *(continued)*			
Strongyloides stercoralis (**strongyloidiasis**)	**Ivermectin** *200* µg/kg/d po x2 d	**Albendazole** 400 mg po bid x2 d (7–10 d for hyperinfection syndrome)	Case report of ivermectin failure in pt with hypogammaglobulinemia *(Am J Med Sci 311 178, 1996)*
Trichostrongylus orientalis	**Albendazole** 400 mg po x1 dose	**Pyrantel pamoate** 11 mg/kg (max 1.0 gm) po x1	**Mebendazole** *100* mg po bid x3 d
Trichuris trichiura (**whipworm**)	**Albendazole** 400 mg po once daily x3 days	**Mebendazole** 100 mg po bid x3 d or 500 mg once	**Ivermectin** 200 µg/kg daily po x3 d
NEMATODES—EXTRAINTESTINAL (Roundworms)			
Angiostrongylus cantonensis—a cause of eosinophilic meningitis	Supportive care. Serial LPs to ↓ intracranial pressure	Antihelminth therapy may worsen meningitis *(NEJM 346 668, 2002)*. Prednisone may help	Mortality rate <1%. Ref: *AJM 114 217, 2003)*
Anisakis simplex (**anisakiasis**)	Physical removal: endoscope or surgery	Questionable response to albendazole *(Ln 360 54, 2002)*	Anisakiasis acquired by eating raw fish: herring, salmon, mackerel, cod, squid. Similar illness due to Pseudoterranova species acquired from cod, halibut, red snapper
Ancylostoma braziliense & caninum causes **cutaneous larva migrans**	**Ivermectin** 200 µg/kg po x1 dose/d x1–2 d	**Albendazole** 200 mg po bid x3 d	Also called 'creeping eruption,' dog and cat hookworm. Ivermectin cure rate 77% (1 dose) to 97% (2–3 doses) *(CID 31 493, 2000)*
Baylisascariasis (Raccoon ascaris)	No drug proven efficacious. Try **albendazole** 25 mg/kg/d x20 d		Usually pediatric problem *(PIDJ 22 651, 2003)*
Dracunculus medinensis: **Guinea worm**	Slow extraction of pre-emergent worm	**Metronidazole** 250 mg po tid x10 d: used to ↓ inflammatory response and facilitate removal. Immersion in warm water promotes worm emergence. Mebendazole 400–800 mg/d x6 d may kill worm	
Filariasis. Wolbachia bacteria needed for filarial development. Rx with doxy 100–*200* mg/d x4–6 wks ↓ number of wolbachia & number of microfilaria *(BMJ 326 207, 2003)*			
Lymphatic (**Elephantiasis**): Wuchereria bancrofti or Brugia malayi or B. timori	**Diethylcarbamazine** 6 mg/kg po once—similar effect as multiple doses[1,2]	**Diethylcarbamazine**[2] (DEC) po over 14 days: Day 1: 50 mg; day 2: 50 mg tid; day 3: 100 mg tid; days 4–14: 2 mg/kg tid	
Cutaneous:			
Loiasis: **Loa loa** eyeworm disease	**Diethylcarbamazine** (DEC)[1,2]—6 mg/kg po x1 dose		DEC 300 mg/wk po effective prophylaxis
Onchocerca volvulus (**onchocerciasis**)—river blindness *(Ln 360 203, 2002)*	**ivermectin** 150 µg/kg po x1 dose, repeat q6 months to suppress dermal and ocular microfilariae. If eye involved: start **prednisone** 1 mg/kg/d po several days before ivermectin. NOTE: Worm survival requires symbiotic bacteria Wolbachia *(Science 296 1365, 2002)*		Ivermectin ↓ number of microfilariae in skin and impairs female worm fertility; does not kill adult worms (nothing does). Ivermectin OK in pregnancy
Body cavity:			
Mansonella perstans (dipetalonemiasis)	**Mebendazole**[1] 100 mg po bid x30 d or **albendazole** 400 mg po bid x10 d	Usually no or vague allergic symptoms + eosinophilia. Ivermectin has no activity against this species	
Mansonella streptocerca	**Diethylcarbamazine**[2] as above for Wuchereria OR **ivermectin** 150 µg/kg x1	Chronic pruritic hypopigmented lesions that may be confused with leprosy. Can be asymptomatic	
Mansonella ozzardi	**ivermectin** 200 µg/kg x1 dose may be effective	Usually asymptomatic. Articular pain, pruritus, lymphadenopathy reported. May have allergic reaction from dying organisms	
Dirofilariasis: **Haartworms**			
D. immitis: dog heartworm	No effective drugs; surgical removal only option		Can lodge in pulmonary artery → coin lesion. Eosinophilia rare
D. tenius (raccoon), D. ursi (bear), D. repens (dogs, cats)	No effective drugs	Worms migrate to conjunctivae, subcutaneous tissue, scrotum, breasts, extremities	
Gnathostoma spinigerum: eosinophilic myeloencephalitis	**Albendazole** *400* mg po qd or bid x21 d	**Ivarmectin** 200 µg/kg/d x2 d	

[1] May need antihistamine or corticosteroid for allergic reaction from disintegrating organisms
[2] Diethylcarbamazine available from Wyeth Ayerst (610) 971-5509
NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. *See page 103 for abbreviations*

TABLE 13A (7)

INFECTING ORGANISM	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
NEMATODES—Extraintestinal (Roundworms) *(continued)*			
Toxocariasis *Clin Micro Rev 16 265 2003*	**Rx directed at relief of symptoms as infection self-limited, e.g., steroids & antihistamines; use of anthelminthics controversial.**		
Visceral larval migrans	**Albendazole** 400 mg po bid x5 d	**Mebendazole** 100–200 mg po bid x5 days	Severe lung, heart or CNS disease may warrant steroids Differential dx of larval migrans syndromes: Toxocara canis and catis Ancylostoma spp, Gnathostoma spp, Spirometra spp
Ocular larval migrans	First 4 wks of illness: (Oral **prednisone** 30–60 mg po qd + subtenon **triamcinolone** 40 mg weekly) x2 weeks		No added benefit of antihelminthic drugs. Rx of little effect after 4 wks
Trichinella spiralis (**trichinosis**) –muscle infection	**Albendazole** 400 mg po bid x8–14 d Concomitant **prednisone** 40–60 mg po qd	**Mebendezole** 200–400 mg po tid x3 d, then 400–500 mg po tid x10 d	Use albendazole/mebendazole with caution during pregnancy
TREMATODES (Flukes)			
Clonorchis sinensis (liver fluke)	**Praziquantel** 25 mg/kg po tid x1 day or **albendazole** 10 mg/kg/d po x7 d		Same dose in children
Fasciola buski (intestinal fluke)	**Praziquantel** 25 mg/kg po tid x1 day		Same dose in children
Fasciola hepatica (sheep liver fluke)	**Triclabendazole**[NUS] (Fasinex, Novartis Agribusiness) 10 mg/kg po x1 dose. Ref: *CID 32:1, 2001*		**Bithionol**[CDC1] Adults and children: 30–50 mg/kg (max dose 2 gm/d) qod x10–15 doses
Heterophyes heterophyes (intestinal fluke) Metagonimus yokogawai (intestinal fluke) Opisthorchis viverrini (liver fluke)	**Praziquantel** 25 mg/kg po tid x1 day		Same dose in children. Same regimen for **Metorchis conjunctus (North American liver fluke)** **Nanophyetus salmincola:** Praziquantel 20 mg/kg po tid x1 d
Paragonimus westermani (lung fluke)	**Praziquantal** 25 mg/kg po tid x2 days or **bithionol**[CDC1] 30–50 mg/kg po x1 qod x10 d		Same dose in children
Schistosoma haemetobium; GU bilharziasis *(NEJM 346:1212, 2002)*	**Praziquantal** 20 mg/kg po bid x1 day (2 doses)		Same dose in children. Alternative: metritonate 10 mg/kg/dose po q2 wks for 3 doses
Schistosoma intercalatum	**Praziquantel** 20 mg/kg po bid x1 day (2 doses)		Same dose in children
Schistosoma japonicum; Oriental schisto. *(NEJM 346:1212, 2002)*	**Praziquantel** 20 mg/kg po **tid** x1 day (**3 doses**)		Same dose in children. Cures 60–90% pts
Schistosoma mansoni (intestinal bilharziasis). Possible praziquantel resistance *(JID 176:304, 1997)* *(NEJM 346:1212, 2002)*	**Praziquantel** 20 mg/kg po bid x1 day (2 doses)	**Oxamniquine**[NUS] single dose of 15 mg/kg po once in North and East Africa 20 mg/kg po daily x3 d. Do not use during pregnancy	Same dose for children. Cures 60–90% pts
Schistosoma mekongi	**Praziquantel** 20 mg/kg po **tid** x1 day (**3 doses**)		Same dose for children
Toxemic schisto. Katayama fever	**Praziquentel** 25 mg/kg po q4h with food x3 doses		Massive infection with either S. japonicum or S. mansoni
CESTODES (Tapeworms)			
Echinococcus granulosus (hydatid disease) *(CID 37:1073, 2003; Ln 362:1295 2003)*	Meta-analysis supports percutaneous aspiration injection-reaspiration (PAIR) + albendazole. Before **and** after drainage **albendazole** >60 kg: 400 mg po bid or <60 kg: 15 mg/kg/d div bid with meals. Then: Puncture (P) & needle aspirate (A) cyst content. Instill (I) hypertonic saline (15–30%) or absolute alcohol & wait 20–30 min, then re aspirate (R) with final irrigation. **Continue albendazole x28 d.** Cure in 96% as compared to 90% pts with surgical resection		
Echinococcus multilocularis (alveolar cyst disease) *(COID 16:437, 2003)*	**Albendazole** efficacy not clearly demonstrated, can try in dosages used for hydatid disease. Wide surgical resection only reliable rx, technique evolving *(Radiology 198:259, 1996)*		
Intestinal tapeworms			
Diphyllobothrium latum (fish), Dipylidium caninum (dog), Taenia saginata (beef), and Taenia solium (pork)		**Praziquantel** 5–10 mg/kg po x1 dose for children and adults. **Alternetiva: Niclosamide** 2 gm po x1	
Hymenolepis diminuta (rats) and H. nana (humans)		**Praziquantal** 25 mg/kg po x1 dose for children and adults. **Alternativa: Niclosamide** 500 mg po qd x3 d	

[1] **CDC** = Available from CDC Drug Service

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. *See page 103 for abbreviations*

TABLE 13A (8)

INFECTING ORGANISM	SUGGESTED REGIMENS: PRIMARY	SUGGESTED REGIMENS: ALTERNATIVE	COMMENTS
CESTODES (Tapeworms) *(continued)*			
Cerebral (neuro) cysticercosis Larval stage of *T. solium*—*see Comment* Management refs: *Ln 361:547, 2003 & Ln ID 2:751, 2002*	Cysticercosis outside CNS—benign—no treatment. Inside CNS—no unanimity. Expert panel: (1) If growing &/or many &/or giant cysts &/or subarachnoid disease: **Treat** (2) Calcified cysticercosis: **no treatment** (3) **Disagreement**: Few viable cysts, degenerating cysts *(see Comment)*	Albendazole cheaper & more effective than praziquantel **Albendazole** 15 mg/kg/d (max 800 mg) in 2 div doses x8 d **OR** **Praziquantel** 50–100 mg/kg/d in 3 div doses x30 d **Anti-seizure mede** for inflamed degenerating cysts	**Daxamethaeone (6 mg/d) ± seizure meds may be needed to control rx-induced inflammation from cyst death.** Viable cyst = hypodense vesicle on CT or hyperintense on MRI T_2-signal. If viable cysts: 10 d of albendazole + dexamethasone ↓ number of viable cysts & number of generalized seizures *(NEJM 350:249, 2004)*
Sparganosis (Spirometra mansonoides) Larval cysts; source—frogs/snakes	Surgical resection or ethanol injection of subcutaneous masses *(NEJM 330:1887, 1994)*		
ECTOPARASITES Ref: *CID 36:1355, 2003; NEJM 346:1645, 2002; Ln 363:889, 2004* **NOTE: Due to potential neurotoxicity, lindane products should only be used as last resort.**			
Pediculus humanus corporis (body lice) P. humanus var. capitis (**head louse**, nits) Phthirus pubis (crabs)	Treat the clothing. Organism lives in deposits eggs in seams of clothing. Discard clothing if not possible; treat clothing with 1% malathion powder or 10% DDT powder **Permethrin** 5% prescription strength (ELIMITE) or 1% non-prescription (Nix). Wash hair, apply lotion for 10 min, then rinse off; comb 2nd treatment 7–10 days after 1st to kill newly hatched lice (all products). **OR ivermectin** 200 µg/kg single dose po in 2 doses 10 days apart. **does not affect nits. OR** (not in neonates/infants) **Malathion 0.5% lotion** (Ovide). Apply for 8–12 hrs. No need to comb for lice after malathion	Body louse leaves clothing only for blood meal. Nits in clothing viable for 1 month. Ref: *Med Lett 38:6, 1997* Benefit of residual permethrin on hair reduced by shampoos or vinegar. No residual effect with lindane or pyrethrin products Nit removal important adjunct. Use nit comb ± enzymatic egg remover (CLEAR is one example) Treat sex partners if body or pubic lice Cost: Permethrin 60 gm $9.20; malathion $31.25; ivermectin $9.97 For failures with 1% permethrin, repeat permethrin + po TMP/SMX 10 mg/kg/d in 2 div doses x10 days *(Ped 107:E30, 2001)*
Sarcoptes scabiei (**ecables**) (mites) *(CID 27:646, 1998)*			
Immunocompetent patients	**Primary: Permethrin** 5% cream (ELIMITE). Apply entire skin from chin to toes. Leave on 8–10 hrs. Repeat in 1 week. Safe for children >2 mos old **Alternative: Ivermectin** 200 µg/kg po x1 *(NEJM 333:26, 1995)* **or** 10% **crotamiton** topically 1x/d x2 d	Trim fingernails. Reapply to hands after handwashing. Pruritus may persist x2 wks after mites gone	
AIDS patients; CD4 <150/mm^3 (Norwegian scabies—*see Comments*)	For Norwegian scabies: **Permethrin** as above on day 1, then 6% sulfur in petrolatum daily on days 2–7, then repeat x several weeks **Ivermactin** 200 µg/kg po x1 reported effective	Norwegian scabies in AIDS pts: Extensive, crusted. Can mimic psoriasis. Not pruritic. ELIMITE 60 gm $18.10; lindane 60 ml $2.60–10.50 Highly contagious—isolate!	

TABLE 13B: DOSAGE, PRICE, AND SELECTED ADVERSE EFFECTS OF ANTIPARASITIC DRUGS

NOTE: Drugs available from CDC Drug Service indicated by CDC. Call (404) 639-3670 (or 2888).
Doses vary with indication. For convenience, drugs divided by type of parasite; some drugs used for multiple types of parasites, e.g., albendazole.
COMMENT: Cost data represent average wholesale prices as listed in 2004 Drug Topics Red Book, Medical Economics.

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE (Cost)	ADVERSE REACTIONS/COMMENTS
Antiprotozoan Drugs		
Intestinal Parasites		
Albendazole (Albenza)	Doses vary with indication. 200–400 mg bid po 200 mg tab $1.50	Teratogenic. Pregnancy Cat. C; give after negative pregnancy test. Abdominal pain, nausea/vomiting, alopecia, ↑ serum transaminase. Rare leukopenia.
Dehydroemetine *(CDC)**	1.5 mg/kg/d to max. of 90 mg IM	Local pain, ECG changes, cardiac arrhythmias, precordial pain, paresthesias, weakness, peripheral neuropathy, GI nausea/vomiting, diarrhea. Avoid strenuous exercise for 4 wks after rx.
Diloxenide furoate *(CDC)**	500 mg po tid	GI flatulence, abdominal distention, nausea/vomiting. Pruritus, urticaria.
Furazolidone (Furoxone)	Peds: 6 mg/kg/d div. qid. Not for infants <1 mo. old. Liquid: 50 mg/15 ml; 473 ml $100	Only liquid antigiardiasis drug in U.S. Disulfiram-like reaction with alcohol. Occasional side-effects: Fever, urticaria, ↓BP, arthralgia, nausea/vomiting, headache. Hemolysis if G6PD deficient. May turn urine brown.
Iodoquinol (Yodoxin) (650 mg $0.93)	Adults: 650 mg po tid, children: 40 mg/kg/d div. tid	Rarely causes nausea, aodominal cramps, rash, acne. Contraindicated if iodine intolerance.
Metronidazole/Ornidazole[NUS] (Tiberal)	Side-effects similar for all. *See metronidazole in Table 10A, page 64, & 10B, page 71.*	
Paromomycin (Humatin) Aminosidine in U.K.	Up to 750 mg qid 250 mg caps $1.90	Drug is aminoglycoside similar to neomycin. If absorbed due to concomitant inflammatory bowel disease can result in oto/nephrotoxicity. Doses >3 gm assoc. with nausea, aodominal cramps, diarrhea.
Quinacrine[NUS] **(Atabrine, Mepacrine)**	100 mg tid. No longer available in U.S.; 2 pharmacies will prepare as a service: (1) Connecticut 203-785-6818; (2) California 800-247-9767	Contraindicated for pts with history of psychosis or psoriasis. Yellow staining of skin. Dizziness, headache, vomiting, toxic psychosis (1.5%), hemolytic anemia, leukopenia, thrombocytopenia, urticaria, rash, fever, minor disulfiram-like reactions.
Tinidazole (Tindamax)	500 mg tabs, with food. Regimen varies with indication. Cost: 2 gm $18.24	Chemical structure similar to metronidazole but better tolerated. Seizures/peripheral neuropathy reported. **Adverse effects:** Metallic taste 4–6%, nausea 3–5%, anorexia 2–3%.
Extraintestinal Parasites		
Antimony compounds[NUS] Stibogluconate sodium (Pentostam, Tricostam) *(CDC)* Meglumine antimonate (Glucaratime, Glucantim—French tradenames)	Solution containing 30–34% pentavalent antimony	Cough/vomiting if IV infusion too fast. Arthralgia 50%. Others: myalgia, bradycardia, cramps/diarrhea, pruritus/rash, renal toxicity, ↑ amylase. **NOTE: EKG abnormalities occur. Combination rx with, or sequentiel rx with, ampho B may trigger fatal arrhythmias *(Ln 351:1928, 1998)*.**
Artesunate[NUS]	Adults: 4 mg/kg/d po x3 d; can give IM	Drug fever, abdominal pain, diarrhea, primary heart block. Refs: *CID 33:2009, 2001; Ln 359:1365, 2002; AAC 46:778, 2002.*
Atovequone (Mepron) Ref: *AAC 46:1163, 2002*	Suspension: 1 tsp (750 mg) po bid 750 mg/5 ml. Cost: 210 ml $744.00	No. pts stopping rx due to side-effects was 9%: rash 22%, GI 20%, headache 16%, insomnia 10%, fever 14%.
Atovaquone and proguenil (Malarone) For prophylaxis of P. falciparum; little data on P. vivax	Prophylaxis: 1 tab po (250 mg + 100 mg) qd with food Treatment: 4 tabs po (1000 mg + 400 mg) once daily with food x3 days. Tabs: Either 250/100 mg or 62.5/25 mg. Peds dosage *footnote 2, page 95* Cost: 250/100 mg tab $5.15	Adverse effects in rx trials: Adults—abd. pain 17%, N/V 12%, headache 10%, dizziness 5%. Rx stopped in 1%. Asymptomatic mild ↑ in ALT/AST. Children—cough, headache, anorexia, vomiting, abd. pain. *See drug interactions, Table 22.* Safe in G6PD-deficient pts. Can crush tabs for children and give with milk or other liquid nutrients.
Benznidazole[NUS] **(Rochagen**, Roche Brazil)	7.5 mg/kg/d po	Photosensitivity in 50% of pts. GI: abdominal pain, nausea/vomiting/ anorexia. CNS: disorientation, insomnia, twitching/seizures, paresthesias, polyneuritis.
Chloroquine phosphate (Aralen)	Dose varies—*see Malaria prophylaxis and rx, pages 95, 96* 500 mg tabs $5.16	Minor: anorexia/nausea/vomiting, headache, dizziness, blurred vision, pruritus in dark-skinned pts. Major: protracted rx in rheumatoid arthritis can lead to retinopathy. Can exacerbate psoriasis. Can block response to rabies vaccine.

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function. See page 103 for abbreviations.

TABLE 13B (2)

CLASS, AGENT, GENERIC NAME (TRADE NAME)	USUAL ADULT DOSAGE (Cost)	ADVERSE REACTIONS/COMMENTS
Antiprotozoan Drugs/Extreintestinel Parasites *(continued)*		
Dapsone Ref *CID 27 191, 1998*	100 mg po qd 100 mg tabs $0 20	Usually tolerated by pts with rash after TMP/SMX Adverse effects nausea/vomiting, rash oral lesions *(CID 18 630 1994)* Methemoglobinemia (usually asymptomatic) if >10–15% stop drug Hemolytic anemia if G6PD deficient Sultone syndrome fever, rash, hemolytic anemia, atypical lym hocytes and liver in ury *(Mest J Med 156 303 1992)*
Eflornithine[NUS] **(Ornidyl)**	Approved in U S for trypanosome infections but not marketed Contact Hoechst Marion Roussel (800) 552-3656	Diarrhea in ½ pts vomiting abdominal pain, anemia/leukopenia in ½ pts seizures alopecia jaundice ↓ hearing
Fumegillin	Eyedrops + po 20 mg po tid Call 800-547-1392	Adverse events Neutropenia & thrombocytopenia
Halofantrine (Halfan)	Adults 500 mg po q6h x3 doses Children 8 mg/kg po q6h x3 doses 250 mg tab $9 88	Poor oral bioavailability ↑ with fatty meal Causes delay in A-V conduction **do not use if long QT interval or pt taking drugs known to ↑ QT interval (e.g., quinine/quinidine, astemizole, chloroquine, antidepressants, neuroleptic drugs).** Other side effects nausea abdominal pain diarrhea Do not use in pregnancy
Mefloquine (Lariam)	One 250 mg tab/week for malaria prophylaxis for rx 1250 mg x1 or 750 mg & then 500 mg in 6–8 hrs 250 mg tab $11 83 In U S 250 mg tab = 228 mg base, outside U S 275 mg tab = 250 mg base	Side-effects in roughly 3% Minor headache irritability insomnia weakness diarrhea Toxic psychosis seizures can occur Teratogenic—do not use in pregnancy Do not use with quinine quinidine or halofantrine Rare Prolonged QT interval and toxic epidermal necrolysis *(Ln 349 101 1997)* Not used for self-rx due to neuropsychiatric side-effects
Melarsoprol *(CDC)* **(Mel B, Arsobal)** (Manufactured in France)	See Trypanosomiasis for adult dose Peds dose 0 36 mg/kg IV then gradual ↑ to 3 6 mg/kg q1–5 days for total of 9–10 doses	Post-rx encephalopathy (10%) with 50% mortality overall risk of death 2° to rx 4–8% Prednisolone 1 mg/kg/d po may ↓ encephalopathy Other Heart damage albuminuria abdominal pain vomiting peripheral neuropathy Herxheimer-like reaction pruritus
Miltefosine[NUS] **(Zentaris, Impavido)**	100–150 mg (approx 2 25 mg/kg/d) po x28 d Cutaneous leishmaniasis 2 25 mg/kg po qd x6 wks	Contact Astra Medica Ger **Pregnancy—No** teratogenic Side-effects vary kala-azar pts vomiting in up to 40%, diarrhea in 17%, mild to moderate in severity—may resolve in <1 day
Nifurtimox (Lampit) *(CDC)* (Manufactured in Germany by Bayer)	8–10 mg/kg/d po div 4x/day	Side-effects in 40–70% of pts GI abdominal pain nausea/vomiting CNS polyneuritis (1/3) disorientation, insomnia, twitchin seizures Skin rash Hemol sis with G6PD deficiency
Nitazoxanida (Alinia)	Oral suspension with 100 mg/ml Take with food	Abdominal pain 7 8%, diarrhea 2 1% vomiting/headache 1 1%
Pentamidine (NebuPent)	300 mg via aerosol q month Also used IM 300 mg $98 75 + admin costs	Hypotension hypocalcemia hypoglycemia followed by hyperglycemia pancreatitis Neutropenia (15%) thrombocytopenia Nephrotoxicity Others nausea/vomiting ↑ liver tests, rash
Primequine phosphate	26 3 mg (=15 mg base) $0 77	In G6PD def pts can cause hemolytic anemia with hemoglobinuria esp African Asian peoples Methemoglobinemia Nausea/abdominal pain if pt fasting *(CID 39 1336 2004)*
Pyrimethamine (Daraprim, Malocida) Also combined with sulfadoxine as **Fansidar**	100 mg po then 25 mg qd 25 mg $0 43 Cost of folinic acid (leucovorin) 5 mg $2 00	Major problem is hematologic megaloblastic anemia ↓ WBC, ↓ platelets Can give 5 mg folinic acid/day to ↓ bone marrow depression and not interfere with antitoxoplasmosis effect If high-dose pyrimethamine ↑ folinic acid to 10–50 mg/d Pyrimethamine + sulfadiazine can cause mental changes due to carnitine deficiency *(AJM 95 112 1993)* Other Rash, vomiting, diarrhea, xerostomia
Quinacrine[NUS]	For giardiasis 100 mg po tid x5 d Peds dose 2 mg/kg po tid (max 300 mg/d) x5 d	Compounded by Med Center Pharm New Haven CT (203) 688-6816 or Panorama Compound Pharm Van Nuys CA (800) 247-9767
Quinidine gluconate	Loading dose of 10 mg (equivalent to 6 2 mg of quinidine base)/kg IV over 1–2 hrs and then constant infusion of 0 02 mg of quinidine gluconate/kg/minute 80 mg IV $21 56	Adverse reactions of quinidine/quinine similar (1) IV bolus injection can cause fatal hypotension (2) hyperinsulinemic hypoglycemia esp in pregnancy (3) ↓ rate of infusion of IV quinidine if QT interval ↑ >25% of baseline (4) reduce dose 30–50% after day 3 due to ↓ renal clearance and ↓ vol of distribution
Quinine sulfate (300 mg salt = 250 mg base)	325 and 650 mg tabs No IV prep in U S Oral rx of chloroquine resistant falciparum malaria 650 mg po tid x3d , then tetracycline 250 mg po qid x7 d 325 mg $0 16	Cinchonism tinnitus headache nausea abdominal pain blurred vision Rarely blood dyscrasias drug fever asthma hypoglycemia Transient blindness in <1% of 500 pts *(AnIM 136 339 2002)*
Spiramycin[1] **(Rovamycine)** *(JAC 42 572 1998)*	Up to 3–4 gm/d	GI and allergic reactions have occurred Not available in U S

[1] Available from FDA (301) 443 5680

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function *See page 103 for abbreviations*

CLASS, AGENT, GENERIC NAME [TRADE NAME]	USUAL ADULT DOSAGE (Cost)	ADVERSE REACTIONS/COMMENTS
Antiprotozoan Drugs/Extraintestinal Parasites *(continued)*		
Sulfadiazine	1 0–1 5 gm po q6h 500 mg $0 34	*See Table 10B page 71 for sulfonamide side effects*
Sulfadoxine and pyrimethamine combination (Fanasidar)	Contains 500 mg of sulfadoxine and 25 mg of pyrimethamine One tab $3 77	Very long mean half-life of both drugs Sulfadoxine 169 hrs pyrimethamine 111 hrs allows weekly dosage Fatalities reported due to Stevens-Johnson syndrome and toxic epidermal necrolysis Renal excretion—use with caution in pts with renal impairment
DRUGS USED TO TREAT NEMATODES, TREMATODES, AND CESTODES		
Bithionol *(CDC)*	Adults & children 30–40 mg/kg (to max of 2 gm/d) po qod x10–15 doses	Photosensitivity skin reactions urticaria GI upset
Diethylcarbamazine[1] (Hetrazan) *(CDC)*	Used to treat filariasis Licensed (Lederle) but not available in U S	Headache dizziness nausea fever Host may experience inflammatory reaction to death of adult worms fever urticaria asthma GI upset (Mazzotti reaction)
Ivermectin (Stromactol, Mectizan)	Strongyloidiasis dose 200 µg/kg x1 dose po Onchocerciasis 150 µg/kg x1 po Scabies 200 µg/kg po x1 3 mg tabs $5 45	Mild side-effects fever pruritus rash In rx of onchocerciasis can see tender lymphadenopathy headache bone/joint pain Can cause Mazzotti reaction *(see above)*
Mebendazole (Vermox)	Doses vary with indication 100 mg tab $5 91	Rarely causes abdominal pain nausea diarrhea Contraindicated in pregnancy and children <2 yrs old
Oxamniquine (Vansil)[NUS]	For S mansoni Some experts suggest 40–60 mg/kg over 2–3 days in all of Africa	Rarely dizziness drowsiness neuropsychiatric symptoms GI upset EKG/EEG changes Orange/red urine
Praziquantel (Biltricida)	Doses vary with parasite, *see Table 13A* 600 mg $11 90	Mild dizziness/drowsiness N/V rash fever Only contraindication is ocular cysticercosis Metab induced by anticonvulsants and steroids can potentiate effect with cimetidine 400 mg po tid
Pyrantel pamoate (over-the-counter as Reese s Pinworm Medicine)	Oral suspension Dose for all ages 11 mg/kg (to max of 1 gm) x1 dose	Rare GI upset headache dizziness rash
Suramin (Germanin) *(CDC)*	For early trypanosomiasis Drug powder mixed to 10% solution with 5 ml water and used within 30 minutes	Does not cross blood-brain barrier no effect on CNS infection Side-effects vomiting pruritus urticaria fever paresthesias albuminuria (discontinue drug if casts appear) Do not use if renal/liver disease present Deaths from vascular collapse reported
Thiabendazole (Mintezol)	Take after meals Dose varies with parasite *see Table 12A* 500 mg $1 25	Nausea/vomiting headache dizziness Rarely liver damage ↓BP angioneurotic edema Stevens-Johnson syndrome May ↓ mental alertness

Abbreviations **Clinde** = clindamycin, **CQ** = chloroquine phosphate, **MO** = metioquine **NUS** = not available in the U S **PO** = primaquine **Pyri** = pyrimethamine **QS** = quinine sulfate **TMP/SMX** = trimethoprim/sulfamethoxazole

[1] Available from Wyeth-Ayerst, (610) 971 5509

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function *See page 103 for abbreviations*

TABLE 14A: ANTIVIRAL THERAPY (Non-HIV)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Adenovirus Cause of RTIs[1] including fatal pneumonia in children & young adults *(CID 35 808 2002)* **Findings include** fever ↑ liver enzymes leukopenia thrombocytopenia diarrhea pneumonia, or hemorrhagic cystitis	**No proven rx. Cidofovir** 5 mg/kg q wk x2 wks then q2 wks + **probenecid** 1 25 gm/M^2 given 3 hrs before cidotovir and 3 & 9 hrs after each infusion *(CID 38 45, 2004)* Successful in 3/8 immunosuppressed children	PCR[2] for adenovirus DNA [+ in 72% of children with 1st infection *(JID 187 311 2003)*] ↑ viral load assoc with fatal outcome in children with stem cell transplant *(CID 35 526, 2002)* ↓ in virus load predicted response to cidotovir *(CID 38 45 2004)*
Coronavirus—SARS-CoV (Severe Acute Respiratory Distress Syn) *(see CID 36 1420 2004)* A new coronavirus isolated in spring 2003 *(NEJM 348 1953 & 1967 2003)* emerged from China (animal reservoir may be civet cat) & spread rapidly from Hong Kong to 32 countries Healthcare workers account for >50% of cases (>90% in Taiwan) *(Ln 361 1319 2003)* Effective adherence to infection control guidelines was likely responsible for finally controlling the epidemic *(Ln 361 1519 2003, NEJM 350 2352 2004)* Only 4 mini-outbreaks in 2004 3/4 from research labs testing live virus *(Science 304 1097 2004)*	Therapy tried or under evaluation *(see Comments)* **Ribavirin**—ineffective Interferon alfa ± steroids—small case series Pegylated INF-α effective in monkeys Value of corticosteroids alone unclear Lopinavir/ritonavir benefit in uncontrolled studies	**Therapy remains predominantly supportive care.**
Enterovirus—Meningitis: most common cause of aseptic meningitis PCR on CSF valuable for early dx *(Scand J Inf Dis 34 359 2002)*	**No rx currently recommanded;** however **pleconaril** (VP 63843) still under investigation [For compassionate use call Viropharma (610) 458 7300 ext 6297 (Donna Kolbush, RN)]	No clinical benefit demonstrated in double-blind placebo controlled study in 21 infants with enteroviral aseptic meningitis *(PIDJ 22 335, 2003)*
Hemorrhagic Fever Virus Infections		
Congo-Crimean Hemorrhagic Fever (HF) *CID 38 1731, 2004*	Oral **ribavirin 30 mg/kg** as initial loading dose & 15 mg/kg q6h x4 days & then 7 5 mg/kg x6 days (WHO recommendation) *(see Comment)*	3/3 healthcare workers in Pakistan had complete recovery *(Ln 346 472 1995)* & 61/69 (89%) with confirmed CCHF rx with ribavirin survived in Iran *(CID 36 1613 2003)*
Ebola/Marburg HF (Central Africa) Epidemic continues in Africa *(JAMA 290 317, 2003)*	**No effective antiviral rx** *(J Virol 77 9733 2003)*	An intense inflammatory response within 4 d after infection may control viral proliferation & result in asymptomatic infection *(Ln 355 2210 2000)* Can infect gorillas & chimps that come in contact with other dead animal carcasses *(Science 303 387, 2004)*
With pulmonary syndrome: Hantavirus pulmonary syndrome, "sin nombre virus" + others now found around the world *(EID 18 768 2002)*	**No benefit from ribavirin has been demonatrated** to date (controlled trial in progress) Refs *JID 173 1297 1996 Emerg Inf Dis 3 95 1997 Curr Inf Dis Rep 3 258 2001*	Acute onset of fever headache myalgias non-productive cough thrombocytopenia and non-cardiogenic pulmonary edema with respiratory insufficiency following exposure to rodents Persistent myalgias nausea diarrhea dramatic (L) shift on blood smear ↓ platelets & ↓ PCO_2 predicted Hanta pulmonary syndrome (HPS) *(CID 34 293 2002)*
With renal syndroma: Lassa Venezuelan Korean HF Sabia Argentinian HF Bolivian HF Junin Machupo	**Ribavirin** IV 2 gm loading dose then 1 gm q6h x4 days then 0 5 gm q8h x6 d *(See Comment Congo-Crimean HF)*	Toxicity low hemolysis reported but recovery when treatment stopped No significant changes in WBC platelets hepatic or renal function Effective in Lassa and in 2 cases of Bolivian HF *(CID 24 718 1997)* No data on others *See CID 36 1254 2003* for management of contacts
Dangue and dangue hemorrhagic fever (DHF) Aedes aegypti major vector *(JID 176 313 1997)* Death rate highest in young children & elderly *(Int J Inf Dis 6 118 2002 CID 35 277 2002)*	**No data on antiviral rx** Fluid replacement with careful hemodynamic monitoring critical *(Ln 352 971, 1998)* Rx of **DHF** with colloids may be more effective than crystalloids in pts with low pulse pressures *(CID 32 204, 2001 J Ped 140 629 2002)* 5 pts with severe **DHF** rx with dengue antibody-neg gamma globulin 500 mg/kg qd IV x3–5 d had rapid ↑ in platelet counts *(CID 36 1623 2003)*	Resurgence in Southeast Asia Central & South America and Caribbean No vaccine best prevention is to limit mosquito contact *(AnIM 128 931 1998 gives specifics BMJ 324 1563 2002)*
West Nile virus *(see AnIM 104 545 2004)* A flavivirus introduced in the U S (NYC) in 1999 transmitted by mosquitoes blood transfusions transplanted organs *(NEJM 348 2196 2003)* & breast-feeding *(MMWR 51 877 2002)* Birds (>200 species) are main host with man & horses incidental hosts In 2003 >7000 cases in U S with 220 deaths with epidemic concentrated in Midwest & mountain states In 2004 ↑ activity in west Usually produces nonspecific febrile disease but 1/150 cases develops meningoencephalitis aseptic meningitis or polio-like paralysis *(AnIM 104 545 2004 JCI 113 1102 2004)*	**No proven rx to date.** 2 clinical trials in progress (1) Interferon alfa-N3 For information see www nyhq org/posting/rahal html *(EID 8 107 2002)* (2) IVIG from Israel with high titer antibody West Nile *(JID 188 5 2003 Transpl Inf Dis 4 160 2003)* Contact NIH 301 496 7453 *see www clinicaltrials gov/show/NCT00068055*	Dx by ↑ IgM in serum & CSF or CSF PCR (contact State Health Dept /CDC) Blood supply now tested in U S & in June–Dec 2003 818 viremic donors identified *(MMWR 53 83 2004)*
Yellow fever	**No data on antiviral rx**	Reemergence across Africa (Uganda 2003) & South America (200 000 cases/yr) Vaccination effective & should be used *(JAMA 276 1157 1996)*
Hepatitis Viral Infections		
Hepatitis A *(Ln 351 1643 1998)*	No therapy recommended If within 2 wks of exposure gamma globulin 0 02 ml/kg IM injection x1 is protective	For vaccine recommendations *see Table 20 (MMWR 48 RR-12 1999)* 40% of pts with chronic Hep C who developed superinfection with Hep A developed fulminant hepatic failure in 1 study *(NEJM 338 286 1998)*
Hepatitis B **Acute**	No therapy recommended	Most common cause of death from acute hepatitis in Italy *(Dig Liver Dis 35 404 2003)*

[1] **RTIs** = respiratory tract infections [2] **PCR** = polymerase chain reaction

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Hepatitis Viral Infectious/Hepatitis B *(continued)*		
Chronic *(AnIM 132 326 2000 NEJM 350 1118 2004 Clin Gastro & Hys 2 87 2004—excellent rx algorithm)* In general, **consider rx in pts with persistent ↑ of aminotransferase; detectable levels of HBsAg in serum; HBV DNA levels of >10^5 copies/ml. Might consider bx if ALT normal & rx if hepatitis present. If <10^5 copies/ml, don't rx unless known significant histological disease. Monitor all HBeAg(+) pts q6–12 months.**	**For HBeAg+, 3 drugs currently FDA-approved:** **Lamivudine (LAV) 100 mg po qd x12 mos. or until 6 mos after HBeAg sero-conversion** **or**	1st line rx well-tolerated & non-toxic but drug resistant YMDD mutations emerge after 1 year rx 15% 2 year rx 38% 3 year rx 56% 4 year rx 67% Mutants less virulent than wild type virus breakthrough associated with flare of hepatitis & occ hepatic decomposition But long-term continuous rx (yrs) improves effectiveness sustained viral response (SVR) delays progression & ↓ incidence of hepatic decomposition & HCC *(NEJM 351 1521 2004)* ($260 for 30-day rx)
	Adefovir (ADF) 10 mg po qd x12 mos. **or**	Recommended if either compensated or uncompensated disease & effective against YMDD mutants (for LAV failures) Well tolerated but must adjust dose for renal impairment (CrCl <50%) More expensive than LAV ($450 for 30 d) & up to 25% show exacerbation of hepatitis after discontinuation No resistance reported to date *(NEJM 348 800 808, 2003)*
	PEG INF alfa–2a 180 μg sq q week (not FDA approved for this indication but once-weekly dosing makes it very attractive) **or**	PEG INF alfa–2a at 90 180 & 270 μg sq q wk was 2x more effective than standard INF 4 5 million units 3x/wk (24% combined response vs 12% p= 036) & will likely replace INF alfa–2b *(J Viral Hepat 10 298 2003)* For HBeAg– PEG INF for 48 wks more effective than LAV alone Combination of both drugs similar to PEG INF alone *(NEJM 351 1206, 2004)*
	Interferon alfa–2b 10 MU 3x/wk or 5 MU daily x16–24 wks. Repeat dosing schedule if HBeAg remains pos but low HBV DNA titers (<10 pg/ml) at end of initial 16 wks	Recommended only for compensated liver disease Do not use if ↑ bilirubin or pro time ↓ albumin history of ascites, encephalopathy or variceal bleeding As with other drugs best response with ↓ HBV DNA (<200 pg/ml) & ↑ ALT (>5x normal) Best HBeAg seroconversion rates of the 3 drugs & shorter duration of rx but multiple side effects [myalgias bone marrow suppression depression (severe) etc.] subcutaneous administration & ↑cost ($1420 for 30 d course)
		Goal of rx: ↓ liver inflammation, stop progression of cirrhosis, & prevent hepatocellular carcinoma. INF lamivudine (LAV) & adefovir (ADF) work response measured by loss of HBeAg ↓ of HBV DNA levels to <20 000 copies/ml or to undetectable return of ALT to normal (41–72%) This usually followed by appearance of HBs antibody loss of HBs Ag & appearance of HBe antibody **Histological improvement seen in 50–60%.** Sustained viral response (**SVR** lack of relapse after rx dc) in pts with loss of both the Ag & HBV DNA occurs in >80% but SVR with persistence of HBV DNA with seroconversion predicts viral relapse **The drugs work best when baseline HBV DNA ↓ & ALT high** *(J Viral Hep 9 208 2002)* SVR after LAV rx with ALT 2x normal = only 5% 2–5x normal 26% >5x normal 64% *(Hepatol 36 186 2002)* SVR also ↑ with ↑ duration of LAV rx 1 year 22% 3 yrs 40% 6 yrs +65% but if ALT >2x normal at initiation of LAV rx SVR 38% 65% & 77% respectively Other nucleoside analogs look impressive [**tenotovir** *(JID 189 1183, 2004)* entecavir *(AAC 46 2525 2002)* emtricitabine]
Prevention Re-infection after transplantation for hepatitis B induced cirrhosis *(See Table 15D page 127 for post-exposure prophylaxis recommendations)*	**Lamivudine** 100 mg qd Start at least 4 wks pre-transplant and continue for at least 12 months post-transplant *(Hpt 30 222A 1999 Trpt 62 1456 1996 Ln 348 1212 1996)*	Based on 3 uncontrolled studies data suggest that lamivudine may reduce the rate of HBV reinfection post-transplant Most pts were clinically stable at 1 yr Post-transplant recurrence of HBV was observed in some pts & YMDD variant HBV was detected in some cases & predicted reinfection in 2 pts *(Hpt 30 222A 1999 J Hpt 34 895 2001)* Lamivudine is most effective in preventing recurrence when combined with HBIG *(Hpt 28 585 1998)* but has been used alone in low-risk pts *(J Hpt 34 888, 2001)* Optimal dose and duration of HBIG unknown
Hepatitis C (up to 3% of world infected 4 million in U.S.) *See AnIM 136 747 2002* www.va.gov/hepatitisc www.hepnet.com/hepc.html		
Acute: Most pts asymptomatic (>75%) occasionally non-specific complaints such as fatigue Anti-HCV antibody may remain undetectable for several months after infection while HCV RNA is positive early mean time to detection 12.6 days in transfusion acquired HCV *(JID 189 3 2004)*	PEG INF + ribavirin as *below*, but remains controversial requires confirmation *(NEJM 346 1091, 2002)*	Early rx of acute hepatitis C with INF alfa–2b may reduce progression to chronic Hep C infection 43/44 pts in Germany with pos HCV RNA (mean 54 days to signs/symptoms of hepatitis and mean 89 days to start of rx after exposure/infection) had neg HCV RNA & normal ALT after 24 wks of INF alfa–2b rx *(NEJM 345 1452 2001)* 5/6 jaundiced pts in Portugal rx with INF alfa–2b for 6 mos had SVR (neg HCV RNA for 1 year) *(Hepatogastroentero 50 1057, 2003)* A review of published trials (206 pts) concluded that SVR following rx of acute Hep C with INF alfa–2b was 32% vs 4% with placebo (p=0 00007) *(Cochrane Database Sys & Rev CD000369 2002)* However spontaneous clearance reported in 24/51 (52%) with symptomatic acute HCV *(Gastroentero 125 80 2003)*
Chronic: *see 2002 NIH consensus statement http://consensus.nih.gov/cons/116/116cdc_intro.html & Semin Liver Dis 23(Suppl 1) 35 2003 & Postgrad Med 114 48 57, 62 2003* **Genotype 1 is most common in U.S. (>90%), & least responsive to rx** Once infected only 15% spontaneously clear virus *(continued on next page)*	**Ref.: www.va.gov/hepatitisc** **Rx recommended for persistent elevations ALT, HCV RNA+, & findings of fibrosis & at least moderate inflammation by liver bx.** *(continued on next page)*	Obtain baseline CBC and at wks 2 & 4 of rx *(see Table 14B page 114)* & HCV RNA at 24 wks hemolytic anemia very common with ribavirin Sustained viral response (SVR) [neg HCV RNA (<50 IU/ml) at least 24 wks after end of rx] assoc with resolution of liver injury & reduction in hepatic fibrosis *(Dig Dis Sci 48 1425 2003)* & **low** likelihood of HCV relapse Rx assoc with ↓ hepatocellular carcinoma *(AnIM 131 174 1999)* & at 8 yrs past INF rx ↓ in liver-related deaths *[RR 0 21 (09– 5)]* esp in those with SVR [RR 03 (003– 2)] *(Hepatol 38 493 2003)* *(continued on next page)*

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14A (3)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS COMMENTS
Hepatitis viral infections/Hepatitis C/Chronic *(continued)*		
(continued from previous page) 85% have chronic infection 15–30% progress to cirrhosis (med time 28–32 yrs) 4% hepatocellular (HCCA) carcinoma 5–10,000 deaths in U S /yr Co-infection with HIV extremely common **Consider dx in high-risk pts *(see Prevention, below)* with ↑ ALT.** Dx made by EIA for HCV antibody sensitivity & specificity >99% in at-risk ppoulations & those with liver disease Qualitative HCV PCR used for confirmation of acute or chronic HIV infection without obvious risk factors or no evidence of liver disease Immunoblot assay used as confirmatory test for pos EIA in non-clinical settings or neg HCV RNA HCV RNA pos 1–3 wks after initial exposure EIA later (>90% by 3 mos) **Persistant infection dx by +HCV PCR for >6 mos.** Progressive liver disease associated with older age, immunosuppressed state (HIV) concurrent Hep B & esp ↑ alcohol use (>30 gm/d) 50% pos for serum cryoglobulins, but clinical manifestations uncommon	**When genotype 1:** **Pegylated INF:** + **Ribavirin** **Wt** **Alfa–2a (Pegasys)** [400 mg a m 180 µg sc q wk 600 mg po p m <75 kg **or** or **Alfa–2b (PEG-Intron)** 600 mg po bid >75kg] 1 5 µg/kg sc q wk **Duration of rx:** **Ganotypa 1: check quantitative HCV RNA after 12 wke. if neg. or ≥2 log ↓: continua for 48 wks (up to 51% SVR reported). If pos. or <2 log ↓: dc rx (unlikaly to reapond & consider rx failure)** *(Hepatol 38 645, 2003, J Hepatol 39 106 2003)* **When genotype 2 or 3 (non-1), alternatives are for 24 wks:** **Standard INF alfa** + **Ribavirin** as with 3 mIU sc 3x/wk Genotype 1 **or** **PEG INF alfa (aithar 2a or 2b)** + **Ribavirin** 400 mg as above po bid [since INF alfa SVR similar to PEG INF for genotypes 2&3]	*(continued from previous page)* 3 large pivotal trials have demonstrated superiority of pegylated interferon + ribavirin over standard interferon ribavirin combination or PEG INF alone [Sustained viral response (SVR) = 42–51% for genotype 1 after 48 wks or 76–82% for genotypes 2 & 3 after 24 weeks] Rates similar with both forms of PEG INF (alfa–2a & alfa–2b) Exceptions are genotypes 2 &3 where PEG INF + ribavirin similar to INF-Rib (76–82% SVR after 24 wks) Factors that ↑ success genotypes other than 1, lower baseline viral levels less fibrosis, lower body wt & surface area *(NEJM 347 975, 2002 Hepatol 38 639, 2003)* Certain genetic markers (HLA class B44) may predict ↑ response *(Am J Gastro 98 1621, 2003)* The rate of SVR in 100 black pts was strikingly lower than in 100 non-Hispanic whites receiving PEG alfa-2a & ribavirin (19% vs 52%, p <0 001) 98% had genotype 1 *(NEJM 350 2265, 2004)* Excessive **alcohol consumption** (>5 oz/d) **acceleretas hepatic fibroala** from HCV *(Ln 349 825 1997)* Occult HBV or HIV infection might account for lack of response to rx in some pts *(NEJM 341 22 1999 CID 36 1564 2003)* **HiV accelarates HCV diaeasa progression** *(CID 33 562, 2001)* & HCV infection ↓ beneficial effects of HAART on HIV progression *(J AIDS 33 365, 2003)* In HIV HCV co-infected pts, SVR substantively better with PEG-INF + ribavirin than with non-PEG INF + ribavirin *(NEJM 351 438, 2004)* Decisions regarding re-treatment of non-responders or relapses complex Only 15–20% of non-responders rx with INF-Rib combination will respond to retreatment with PEG INF-Rib However 61% of those with virologic relapse rx with 1 yr of INF-Rib had SVR vs 21% for INF alone *(Liver Int 23 255 2003)* Response is independent of ribavirin dose *(J Viral Hepat 10 215 2003)* Pts with advanced fibrosis/cirrhosis have ↑ risk of hepatic decompensation & should be re-treated *(2002 NIH Consensus Conference)* Maintenance rx with low-dose pegylated INF currently being studied in non-responders with advanced fibrotic liver diseases *(Curr Hep Rept 3 23 2004)* Some suggest longer rx with PEG INF + Rib may improve SVR for Genotype 1 *(JID 189 964 2004)* Side effects significant 10–14% receiving PEG INF-Rib dc rx 2° to side effects (flu-like symptoms hematological & neuropsychiatric abnormalities **2002 FDA warning:** Intron can cause or aggravate life-threatening neuropsychiatric autoimmune ischemic & infectious disorders—monitor closely) *See drug section Table 14B* **Ribavirin is teratogenic & must not be used if pregnancy possibla in pt or partner** Because of toxicity rx of pts with minimal inflammation by liver bx or low to normal ALT is usually **not** recommended
Occult HCV infection (HCV Ab & HCV PCR both neg) may account for persistent ↑ liver enzymes (ALT &/or GGT) in pts in whom other liver disease excluded 57/100 such pts had HCV RNA found on liver bx & 70% of these had HCV RNA identified in PBMC *(JID 189 3 & 7 2004)* ≥80% adherence to rx regimens assoc with improved SVR but adherence often a problem in this pt population multi disciplinary team aporoach suggested *(Curr Hep Rept 3 10 2004)* Routine screening for HCV infection currently not recommended by U S Preventive Services Task Force *(AnIM 140 462, 2004)*		
Prevantion of acute and chronic infection *(For comment on Hepatitis C prophylaxis, see Table 15D page 127)*		
Herpesvirus infactions *(see review JID 26 541 1998)*		
Cytomegalovirus (CMV)		
Normal host	No rx for acute mononucleosis-like syndrome and not established for congenital CMV *(see Comment)*	A study of newborns with symptomatic congenital CMV infection suggests 8 and 12 mg/kg/d of IV ganciclovir has limited efficacy but ↓ platelets and ↓ PMNs common *(JID 175 1080 1997)*
Immunocompromiaed host	**Treatmant of AIDS patiants with highly activa antiretroviral therapy (HAART) is effective in reducing mortality in pts with CMV infection by 81% *(CID 37: 1365, 2003)* and in suppressing CMV viramia;** 16/16 pts became CMV negative by PCR without specific CMV therapy and none developed retinitis *(AIDS 13 1203 1999)* Monitoring CMV DNA of value in organ transplant pts CMV DNA level ≥13 pg/ml correlated with active infection *(JID 186 829, 2002)*	
Colitis/asophagitis	**Ganciclovir** as with retinitis except induction period extended for 3–6 wks No agreement on use of maintenance *(AnIM 158 957 1998)* Responses less predictable than for retinitis *(AJM 98 109 1995)* **Foscarnet** 90 mg/kg q12h effective in 9/10 pts *(AAC 41 1226 1997)* **Valganciclovir also likely effective.** Switch to oral valganciclovir when po tolerated	
CMV of tha narvous system: Encephalitis & ventriculitis Treatment not defined, but disease develops while taking ganciclovir as suppressive therapy		
Lumbosacral poly radiculopathy	**Ganciclovir** *, as with retinitis* Consider combination of ganciclovir and foscarnet if prior CMV rx used Switch to valganciclovir when possible	Abouf 50% will respond *(CID 20 747 1995)* survival ↑ (5 4 wks to 14 6 wks) *(CID 27 345 1998)*
Monopeuritis multiplex	Not defined	Due to vasculitis and may not be responsive to antiviral rx *(AnNeurol 29 139, 1991)*

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infectiona/Cytomegalovirus *(continu=>*		
CMV pneumonia—seen predominantly in transplants (esp bone marrow) rare in HIV	**Ganciclovir** 5 mg/kg IV q12h x3 wks followed by maintenance valganciclovir 900 mg po qd or ganciclovir 5 mg/kg IV qd	11/16 pts showed initial improvement with either ganciclovir or foscarnet but disease eventually progressed despite maintenance *(CID 23 76 1996)* In BMT recipients serial measure of pp65 antigen was useful in establishing early dx of CMV interstitial pneumonia with good results if GCV was initiated within 6 days of antigen positivity *(Bone Marrow Transplant 26 413 2000)* For preventive therapy *see Table 15E page 129*
Retinitis (most common in AIDS) Differential dx HIV retinopathy herpes simplex retinitis varicella-zoster retinitis (rare hard to diagnose) *(Ophthal 111 1326 2004)* 33–63% with inactive CMV retinitis who respond to HAART (↑ of ≥60 CD4 cells/ml) devel immune recovery vitreitis (vision ↓ & floaters —with posterior segment inflammation—vitreitis papillitis & macular changes) an avg of 43 wks after rx started *(JID 179 697 1999 AIDS 14 1163, 2000, CID 36 1063 2003)* Continued ophthalmologic follow-up needed Corticosteroid rx ↓ inflammatory reaction of immune recovery vitreitis without reactivation of CMV retinitis *(5th CRV Abst 751)* *See Guidelines of International Panel (ArIM 158 957 1998)*	**Induction therapy, primary Valganciclovir** 900 mg po bid with food x 21 days **OR ganciclovir** (GCV) 5 mg/kg IV q12h (adjust for renal function) x14–21 days **OR foacarnat** (FOS) 90 mg/kg q12h (adjust for renal function) IV at constant rate (requires infusion pump) over minimum of 1 hr x14–21 days **OR** combination of **intraocular ganciclovir (GCV) implant** (delivers 1–2 µg/hr x6–7 mos) + (either concomitant **IV GCV** 5 mg/kg IV qd or **oral valganciclovir** 900 mg qd with food) **Induction therapy, alternative: Cidofovir** 5 mg/kg IV q week x2 wks with **probenecid** (2 gm po 3 hrs before cidofovir dose 1 gm 2 hrs immediately after dose and 1 gm 8 hrs after dose) and 1 liter of normal saline IV 1 hr before cidofovir infusion *(AIDSHR 17 339 1998 Blood 97 388 2001)* **OR fomivirsen** 330 mg by direct intravitreal injection q2wk x2 then q month in combination with valganciclovir as above **OR** for pts who fail monotherapy with GCV or FOS consider combination rx with both (1) **GCV** 5 mg/kg q12h or q24h IV and (2) **FOS** 90 mg/kg q12h up to total of 125 mg/kg qd *(CID 34 1337 2002)* **Suppression** (maintenance therapy) *See CID 28 534 1999* With immune reconstitution from response to HAART USPHS/IDSA guidelines recommend suppressive rx may be dc if **CD4 >100/mm³ after 6 mos of HAART***(see www.aidsinfo.nih.gov for guidelines)* and retinitis inactive **Primary suppression/prophylaxis: Valganciclovir** 900 mg po qd **OR GCV** 5 mg/kg IV qd or 6 mg/kg IV qd 5 days/week **OR FOS** 90–120 mg/kg/day IV with hydration and dose adjusted for renal function (NOTE oral and IV hydration found equally effective 1700 ml/day **Alternative:** Combination of **GCV intraocular implant** q6 mos + **valganciclovir** 900 mg po qd **OR cidofovir** 5 mg/kg IV q2 wks + probenecid & hydration (as above under induction rx)	Cannot use GCV ocular implant alone as approx 50% risk of CMV retinitis other eye at 6 mos & 31% risk visceral disease Risk ↓ with systemic rx *(NEJM 337 83 1997)* Similarly intraocular injections of fomivirsen will not prevent contralateral eye or systemic/visceral disease *(Am J Ophth 133 467 475 484 552 2002)* **Concurrent systemic rx recommended! Fomivirsen** may have a role if isolates become resistant to other therapies Watch for retinal detachments 50–60% within 1 yr of dx of retinitis Equal efficacy of IV GCV and FOS GCV avoids nephrotoxicity of FOS FOS avoids bone marrow suppression of GCV **Oral valganciclovir should replace both.** Emergence of resistance to GCV & valganciclovir minimal even with prophylactic use *(JID 189 1615 2004)* Reports indicate success of combination rx with GCV at 5 mg/kg q24h & FOS up to 125 mg/kg/d for GCV resistant isolates in solid organ transplants *(CID 34 1337 2002)* Hypomagnesemia common complication Valganciclovir 900 mg qd has similar efficacy (17% progressed over 1 year) & toxicity profile as IV ganciclovir but with fewer IV related events *(J AIDS 30 392 2002)*
EBV—Mononucleosis *(NEJM 343 481 2000 Ln ID 3 131 2003)*	**No treatment** Corticosteroids for tonsillar obstruction of airway or CNS complications	Acyclovir and prednisolone inhibited oropharyngeal EBV replication but did not affect duration of symptoms *(Curr Inf Dis Rept 6 200 2004)* Valacyclovir terminated EBV replication & resolved oral hairy leukoplakia in 16/18 cases but recurrence with termination of rx in 1/3 of cases *(JID 188 883 2003, JID 190 387, 2004)*
HHV-6 *(see excellent review PIDJ 21 563, 2002)* [implicated as cause of roseola (exanthem subitum) & other febrile diseases of childhood 80–90% infants infected during 1 year of life & 100% by 2 yrs] Fever & rash documented in transplant pts *(JID 179 311, 1999)* 38% of 82 HHV 6 seropositive BMT pts in Japan had HHV-6 viremia 2–4 wks after transplant ½ had rash *(JID 185 847 2002)* A single immunocompetent pt with HHV-6 associated encephalomyelitis responded to cidofovir followed by ganciclovir *(EID 10 729 2004)* Foscarnet rx improved thrombotic microangiopathy due to HHV-6 *Am J Hematol 76 156 2004*		
HHV-7—ubiquitous virus (>90% of the population is infected by age 3 yrs) No relationship to human disease Infects CD4 lymphocytes via CD4 receptor transmitted via saliva		
HHV-8 (The agent of Kaposi's sarcoma Castleman's disease & body cavity lymphoma)— may cause interstitial pneumonia Transmission within families & heterosexual partners probably via saliva *(CID 37 82 2003)*	**No antiviral treatment** currently recommended Effective anti HIV rx may help	Localized lesions radiotherapy, laser surgery or intralesional chemotherapy Systemic chemotherapy Remission in 5 pts given foscarnet 80 mg/kg/d *(Scand J Inf Dis 26 749 1994)* Castleman's disease has responded to ganciclovir *(Blood 103 1632, 2004)*
Herpes simplex virus (HSV Types 1 & 2) *(See Ln 357 1513 2001)*		
Bell's palsy (May also be caused by H zoster Lyme disease, HHV-6) *(CID 30 529 2000)*	**Either [Acyclovir** (400 mg po 5x/d for 10 days)] with or without [**prednisone** po (30 mg bid or 1 mg/kg daily dose given bid x5 d , then taper to 5 mg bid and dc after total of 10 days)] **or no rx.**	HSV-1 genomes in facial nerves of 11/14 pts by PCR *(AnIM 124 27, 1996)* 99 pts with symptoms <3 days had better recovery and less neural degeneration when rx with acyclovir + prednisone compared to prednisone alone *(Ann Oto/Rhino/Laryngol 105 371, 1996)* but another study was inconclusive More data needed *(Cochrane Database Syst Rev CD001869 2004)* If caused by VZV (Ramsay Hunt syndrome), acyclovir may help *(PIDJ 21 615 2002)*

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14A (5)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus infections/Herpes simplex virus (HSV types 1 & 2) *(continued)*		
Encephalitis *(Excellent reviews CID 35 254, 2002)* UK experience *(EID 9 234 2003)*	**Acyclovir** IV 10 mg/kg IV (infuse over 1 hr) q8h x14–21 days	HSV-1 is most common cause of sporadic encephalitis Survival & recovery from neurological sequelae are related to mental status at time of initiation of rx **Early dx and rx imperative** Mortality rate reduced from >70% to 19% with acyclovir rx PCR analysis of CSF for HSV-1 DNA is 100% specific & 75–98% sensitive 8/33 (25%) CSF samples drawn before day 3 were neg by PCR neg PCR assoc with ↓ protein & <10 WBC/mm^3 in CSF *(CID 36 1335, 2003)* All were + after 3 days CSF IgG Ab usually appears late (>1st week) Dose Up to 20 mg/kg q8h in children <12 yrs Relapse after successful rx reported in 7/27 (27%) children Relapse was associated with a lower total dose of initial acyclovir rx (285 ± 82 mg/kg in relapse group vs 462 ± 149 mg/kg, p <0.03) *(CID 30 185, 2000)* ↓ CSF glucose reported *(CID 38 1506 2004)*
Genital, Immunocompetent **Primery (initial episode)** See excellent reviews *NEJM 350 1970, 2004 &* ***AnIM 137:257, 2002 or CDC 2002 Guidelines***	**Acyclovir** (Zovirax or generic) 400 mg po tid x7–10 days (FDA-approved dosage is 200 mg 5x/d po x10 days) (NB $60/course G $20/course) OR	↓ by 2 days time to resolution of signs & symptoms ↓ by 4 d time to healing of lesions ↓ by 7 d duration of viral shedding Does not prevent recurrences For severe cases only 5 mg/kg IV q8h x5–7 days
	Valacyclovir (Valtrex) 1000 mg po bid x10 days ($134/course) or	An ester of acyclovir which is well absorbed bioavailability 3–5x greater than acyclovir Found to be **equal to acyclovir** *(Sex Trans Dis 24 481 1997)*
	Famciclovir (Famvir) 250 mg po tid x7–10 days (not FDA-approved for this indication) ($64–92/course)	Metabolized to penciclovir which is active component Side effects and activity similar to acyclovir Famciclovir 250 mg po tid found to be **equal to acyclovir** 200 mg 5x/d
Episodic recurrances	**Acyclovir** 400 mg po tid **x5 days** or 800 mg tid po **x2 days** **famciclovir** 125 mg po bid **x5 daya** or **valacyclovir** 500 mg po bid **x3 daye**	All effective with few differences Choice can be made on basis of cost & convenience Trend is to ↓ duration of rx The 2-day course of acyclovir ↓ duration of episode & lesions from 6 to 4 days vs placebo & viral shedding from 58 to 25 hrs *(CID 34 944 2002)* The 3-day course of valacyclovir was equivalent to 5 days duration of episode & lesions 4 4 days *(CID 34 958, 2002)*
Chronic auppresaion *(JAMA 280 928 1998 JID 178 603 1998)* Decision to rx arbitrary but rx sig improves quality of life over 1 yr (*Sex Trans Infect 75 398 1999*)	**Supprasaiva rx reduces the frequency of ganital herpes recurrencaa by 70–80% among pts who hava frequent recurrencaa (i.a., >6 racurrencaa/yr) & many report no symptomatic outbraake** *(MMWR 51 RR-6 2002)* **Acyclovir** 400 mg po bid (cost/yr $1511) **or famciclovir** 250 mg po bid (cost/yr $2686) **or valacyclovir** 1 gm po qd ($2449/yr) for pts with <9 recurrences/ yr use 500 mg po qd ($1650/yr) May use 1 gm po qd it breakthrough at lower dose	All suppress subclinical HSV-2 shedding between episodes of active disease (80–94% ↓ in number of days with subclinical shedding) and ↓ symptomatic recurrences Vala ↓ risk of transmission by 75% vs placebo *(NEJM 350 11 & 67 2004)* Drug resistance unlikely to develop with ↑ use 0.2% after 20 yrs of use in immunocompetent pts However in immunocompromised pts (HIV+ & BMT) 6–7% HSV are resistant *[Clin Micro Rev 16 114 2003 AnIM 163 76 2003]* Since in a large natural hx study 2/3 of pts demonstrated ↓ in recurrences between yrs 1 & 5 (approx median 6 to 3 episodes/ yr) daily suppressive rx should be reassessed periodically and after 3–5 yrs episodic rx may become more practical *(AnIM 131 14, 1999)*
Gingivostomatitis primary (children)	**Acyclovir** 15 mg/kg po 5x/d x7 d	Efficacy demonstrated in randomized double blind placebo-controlled trial *(BMJ 314 1800 1997)*
Kerato-conjunctivitis and recurrent epithelial keratitis	**Trifluridine** (Viroptic) 1 drop 1% solution q2h (max 9 drops/d) for max of 21 days *(see Table 1, page 9)*	In controlled trials, response % > idoxuridine Suppressive rx with acyclovir (400 mg bid) reduced recurrences of ocular HSV from 32% to 19% over 12-month period *(NEJM 339 300 1998)*
Mollaret s recurrent aseptic meningitis (usually HSV-2) *(Ln 363 1772, 2004)*	No controlled trials of antiviral rx & resolves spontaneously In severe cases IV acyclovir or valacyclovir or famciclovir reasonable Daily suppression rx might ↓ frequency of recurrence but no clinical trials	Pos PCR for HSV in CSF confirms dx *(EJCMID 23 560 2004)*
Mucocutaneous **Oral labial, "faver bliatere":** **Normal host** *See Ann Pharm Ther 38 705 2004 J Anti micro & Chemo Ther 3 703 2004*	Start rx with prodrome symptoms ((tingling or burning) before lesions appear **Drug** — **Dose** — **Cost** — **Duration Sx** **Oral:** Valacyclovir — 2 gm po q12h x1 d — $36 — ↓ 1 day Famciclovir[1] — 500 mg po bid x7 d — $112 — ↓ 2 days Acyclovir[NF/OA] — 400 mg po 5x/d (q4h while awake) x5 d — $18 (generic) — ↓ ½ day **Topical:** Penciclovir 1% cream — q2h during day x4 d — $23 — ↓ 1 day Docosanol 10% cream — 5x/d until healed — $13 — ↓ ½ day Acyclovir 5% cream[2] — 6 x/d (q3h) x7 d — $25/3 gm, $78/5 gm — ↓ ½ day [1] FDA approved only HIV [2] Approved for immunocompromised	Penciclovir *(J Derm Treat 13 67 2002 JAMA 277 1374 1997 AAC 46 2848 2002)* Docosanol *(J Am Acad Derm 45 222 2001)* Oral acyclovir 5% cream *(AAC 46 2238 2002)* Oral famciclovir *(JID 179 303 1999)* Topical fluocinonides (0.05% Lidex gel) q8h x5 d in combination with famciclovir ↓ lesion size and pain when compared to famciclovir alone *(JID 181 1906 2000)*

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** name brand **G** generic

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infections/Herpes Simplex Virus (HSV Types 1 & 2)/Mucocutaneous/Oral labial, "fever blisters" *(continued)*		
Herpes Whitlow	*See Table 1, page 18*	
Oral labial or genital: **Immunocompromised (includes pts with AIDS) and critically ill pts in ICU setting** *(See Comment)*	**Acyclovir** 5 mg/kg IV (infused over 1 hr) q8h x7 d (250 mg/M²) or 400 mg po 5x/d x14–21 d *(see Comment if suspect acyclovir resistant)* **OR Famciclovir:** In HIV infected 500 mg po bid for 7 d for recurrent episodes of genital herpes **OR Valacyclovir:** In HIV infected 500 mg po bid for 5–10 d for recurrent episodes of genital herpes or 500 mg po bid for chronic suppressive rx	Acyclovir resistant HSV occurs esp in large ulcers Most will respond to **IV foscarnet** but recur after drug discontinued [median 6 weeks *(NEJM 325 551 1991)*] Suppressive rx with famciclovir (500 mg po bid) reduced viral shedding and clinical recurrences (total days with lesions 18% vs 73% in HIV infected pts *(AnIM 128 21 1998)* similar to findings with acyclovir & valacyclovir 500 mg po bid [at 6 mos 65% of vala-rx were recurrence free vs 26% of placebo-rx *(JID 188 1009 2003)*] Cidofovir (topical) has been used with moderate success *(JID 176 892 1997)*
Perinatal (genital in pregnancy at delivery)	In 25% HSV reactivated in last month of pregnancy Infant exposure to primary lesion 50% risk if recurrent lesion 4% 50% mortality in infected neonates If visible genital lesion deliver by **C-section** regardless of duration of membrane rupture If no lesions or symptoms vaginal delivery Routine HSV cultures no longer recommended **Acyclovir** useful in dose of 10 mg/kg (20 mg/kg if premature) q8h x10–21 days IV *(PIDJ 14 827 1995, NEJM 337 509, 1997)*	
Herpes simiae—Monkey bits (Herpes B virus) *CID 35 1191, 2002*	**Postexposure prophylaxis:** Valacyclovir 1 gm po q8h x14 d or acyclovir 800 mg po 5x/d x14 d **Treatment of disease:** (1) CNS symptoms absent Acyclovir 12.5–15 mg/kg IV q8h or ganciclovir 5 mg/kg IV q12h (2) CNS symptoms present Ganciclovir 5 mg/kg IV q12h	Fatal human cases of myelitis and hemorrhagic encephalitis have been reported following bites scratches or eye inoculation of saliva from monkeys Initial sx include fever headache myalgias and diffuse adenopathy Incubation period of 2–14 days *(EID 9 246 2003)*
Herpes Varicella-Zoster Virus (VZV)		
Varicella		
Normal host (chickenpox) Child (2–12 years)	**Rx not recommended** by American Academy of Pediatrics Oral acyclovir recommended for healthy persons at ↑ risk for moderate to severe varicella i.e. >12 yrs of age chronic cutaneous or pulmonary diseases chronic salicylate rx (↑ risk of Reye syndrome) use **acyclovir 20 mg/kg** po qid x5 days (start within 24 hrs of rash)	Modest response to acyclovir Slowed development and ↓ number of new lesions duration of disease ↓ in children receiving acyclovir in Europe 7.6 vs 9.0 days *(PIDJ 21 739 2002)* Analgesic requirements decreased *(NEJM 325 1539 1991)* Oral dose of acyclovir in children should not exceed 80 mg/kg/d or 3200 mg/d
Adolescents young adults	**Acyclovir** 800 mg po 5x/d x5–7 days (start within 24 hrs of rash) or **valacyclovir**[NFDA†] 1000 mg po 3x/d x5 d) **Famciclovir**[NFDA†] 500 mg po 3x/d also probably effective but data lacking *(AnIM 130 922 1999)*	↓ duration of fever time to healing and symptoms *(AnIM 117 358 1992)*
Pneumonia or chickenpox in 3rd trimester of pregnancy	**Acyclovir** 800 mg po 5x/d or 10 mg/kg IV q8h x5 days Risks and benefits to fetus and mother still unknown Many experts recommend rx especially in 3rd trimester Some would add VZIG (varicella zoster immune globulin)	Varicella pneumonia severe in pregnancy (41% mortality *Ob Gyn 25 734 1965)* and acyclovir ↓ incidence and severity *(JID 185 422 2002)* If varicella susceptible mother exposed and respiratory symptoms develop within 10 days after exposure start acyclovir *(CCTID 13 123 1993)* Acyclovir is pregnancy category B no evidence of ↑ birth defects *(MMWR 42 806 1993)*
Immunocompromised host	**Acyclovir** 10–12 mg/kg IV (infused over 1 hr) q8h x7 days (500 mg/M²)	Continuous infusion of high-dose acyclovir (2 mg/kg/hr) successful in 1 pt with severe hemorrhagic varicella *(NEJM 336 732, 1997)* Mortality high (43%) in AIDS pts *(Int J Inf Dis 6 6, 2002)*
Prevention Varicella is the leading cause of vaccine-preventable deaths in children in the U.S. *(MMWR 47 365 1998)*	**CDC Recommendations for Prevention:** Since <5% of cases of varicella but >50% of varicella-related deaths occur in adults >20 yrs of age the CDC recommends a more aggressive approach in this age group **1st, varicella-zoster immune globulin** (VZIG) (125 U/10 kg (22 lbs) body weight IM up to a max of 625 U minimum dose is 125 U) is recommended for post-exposure prophylaxis in susceptible persons at greater risk for complications (immunocompromised such as HIV malignancies pregnancy and steroid rx) as soon as possible after exposure (<96 hrs) If varicella develops initiate rx quickly (<24 hrs of rash) with **acyclovir** as below Some would rx presumptively with acyclovir in high risk pts **2nd,** susceptible adults should be vaccinated Check antibody in adults with negative or uncertain hx of varicella (10–30% will be Ab-neg.) and vaccinate those who are Ab-neg **3rd,** susceptible children should receive vaccination Recommended routinely before age 12–18 mos but OK at any age	

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function
* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14A (7)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Herpesvirus Infections/Herpes Varicella-Zoster Virus (VZV) *(continued)*		
Herpes zoster (shingles) *(See NEJM 342 635, 2000 & 347 340, 2002)*		
Normal host Effective rx most evident in pts >50 yrs *(For rx of post-herpetic neuralgia, see CID 36 877, 2003)* 25-fold ↓ in zoster after immunization *(MMWR 48 R-6, 1999)*	**[NOTE: Trials showing benefit of rx: only in pts treated within 3 days of onset of rash]** **Valacyclovir** 1000 mg po tid x7 days (adjust dose for renal failure) **OR**	Valacyclovir ↓ post-herpetic neuralgia more rapidly than acyclovir in pts >50 yrs of age; median duration of zoster-associated pain was 38 days with valacyclovir and 51 days on acyclovir *(AAC 39 1546, 1995)* Toxicity of both drugs similar *(Arch Fam Med 9 863, 2000)*
	Famciclovir 750 mg po qd or 500 mg bid or 250 mg 3x/d x7 d; equal efficacy *(J Clin Virol 29 248, 2004)* Adjust for renal failure *(see Table 17)* **OR**	Time to healing more rapid. Reduced post-herpetic neuralgia (PHN) vs placebo in pts >50 yrs of age; duration of PHN with famciclovir 63 days, placebo 163 days. Famciclovir similar to acyclovir in reduction of acute pain and PHN *(J Micro Immunol Inf 37 75, 2004)*
	Acyclovir 800 mg po 5x/d x7–10 days [**Prednisone** po 30 mg bid days 1–7, 15 mg bid days 8–14 and 7.5 mg bid days 15–21 also recommended by some authorities in pts >50 yrs of age *(NEJM 335 32, 1996)*] and especially when pt has large number of lesions (>21) and/or severe pain at presentation *(JID 179 9, 1999)*	A meta-analysis of 4 placebo-controlled trials (691 pts) demonstrated that acyclovir accelerated by approx 2-fold pain resolution by all measures employed and reduced post herpetic neuralgia at 3 & 6 mos *(CID 22 341, 1996)*; med. time to resolution of pain 41 days vs 101 days in those >50 yrs. Prednisone added to acyclovir improved quality of life measurements (↓ acute pain, sleep, and return to normal activity) *(AnIM 125 376, 1996)*. In post-herpetic neuralgia, controlled trials demonstrated effectiveness of gabapentin, the lidocaine patch (5%) & opioid analgesic in controlling pain *(Drugs 64 937, 2004; J Clin Virol 29 248, 2004)*. Nortriptyline & amitriptyline are equally effective but nortriptyline is better tolerated *(CID 36 877, 2003)*
Immunocompromised host Not severe	**Acyclovir** 800 mg po 5x/d x7 d (**Options: Famciclovir** 750 mg po qd or 500 mg bid or 250 mg 3x/d x7 d **OR valacyclovir** 1000 mg po tid x7 d; though both are not FDA-approved for this indication)	If progression, switch to IV
Severe, >1 dermatome, trigeminal nerve or disseminated	**Acyclovir** 10–12 mg/kg IV (infusion over 1 hr) q8h x7–14 days. In older pts, ↓ to 7.5 mg/kg. If nephrotoxicity and pt improving, ↓ to 5 mg/kg q8h	A common manifestation of immune reconsfitution following HAART in HIV-infected children *(J All Clin Immunol 113 742, 2004)* Rx must be begun within 72 hrs. Acyclovir-resistant VZV occurs in HIV+ pts previously treated with acyclovir. Foscarnet (40 mg/kg IV q8h for 14–26 days) successful in 4/5 pts but 2 relapsed in 7 and 14 days *(AnIM 115 19, 1991)*
Influenza (A & B) *(CID 35 729, 2002)* **Suepect or proven acute disease** Rapid diagnostic tests available *(J Clin Virol 25, 15, 2002)*; antiviral rx cost effective without viral testing in febrile pt with typical symptoms during influenza season *(Am J Med 113 200, 2002)* Highly pathogenic avian influenza (H5N1) now in poultry (mainly chickens & ducks) in East & Southeast Asia; >100 million chickens died or were slaughtered & 23 of the 34 human cases died *(LnID 4 261, 2004)*. Little evidence of human-to-human transmission; most have had direct contact with poultry (median time 3 days) *(NEJM 350 1179, 2004)*. Human isolates demonstrate resistance to amantadine/rimantadine. Oseltamivir rx recommended if avian H5N1 suspected *(MMWR 53 97, 2004)*	**If fever & cough: known community influenza activity: and 1et 48 hrs of illnesa, conaider:** **For influenza A & B; also avian (H5N1)** **Oseltamivir** 75 mg po bid x5 d (also approved for rx of children age 1–12 yrs; dose 2 mg/kg up to a total of 75 mg bid x5 d.) or **Zanamivir** 2 inhalations (2x5 mg) bid x5 d	**For influenza A only:** **Rimantadine** or **amantadine**—Age 1–9 yrs: 5 mg/kg/d to max of 75 mg po bid 10–65 yrs: 100 mg po bid >65 yrs: 100 mg po qd (adjust for ↓ renal function) for **3–5 d. or 1–2 d after tha diaappaarance ot aymptoma.**	Pts with COPD or asthma: **potantial risk ot bronchospasm with zanamivir**. If using inhaled bronchodilator, use before dose of zanamivir. Amantadine & rimantadine equally effective, but rimantadine ↓ side effects *(Cochrane Database Sys Rev CD 001169, 2004)*. All ↓ duration of symptoms by approx. 50% (1–2 d.) if given within 30–36 hrs after onset of symptoms. Benefit influenced by duration of sx before rx; initiation of oseltamivir within 1st 12 hrs after fever onset ↓ total median illness duration by 74.6 hrs (3.1 days, 41%) more than if given after 48 hrs of fever *(JAC 51 123, 2003)*. **Disturbing report** of oseltamivir-resistant virus 1st detected after 4 days of rx & continued to shed potentially infectious virus *(Ln 364 733 & 759, 2004)*. Whether these resistant viruses are transmissible is unknown. In another study of 298 rx cases of adults & children, no oseltamivir-resistant viruses found *(JID 189 440, 2004)*
Pravention *See MMWR 52 RR-8, 2003 & RR-6 1, 2004* Annual vaccination recommended (preferably Oct.-Nov.) for >65 yrs age, residents of nursing homes or chronic care facilities that house persons with chronic medical conditions, those with chronic pulmonary or cardiac conditions, chronic metabolic diseases (diabetes, renal failure, etc.), immunosuppression, children on chronic ASA, women in 2nd or 3rd trimester or persons who can transmit virus to above (HCWs, etc.)	**Prevantion of influanza A & B** give vaccine and if ≥13 yrs age, consider **oseltamivir** 75 mg po qd for duration of peak influenza in community or for outbreak control in high risk populations *(CID 39 459, 2004)* (Consider for similar populations as immunization recommendations.)	**Pravention ot influenza A:** give vaccine followed by **rimantadine** or **amantadina** (dosages as above) for duration of influenza A activity in community or for outbreak control in high risk populations *(CID 39 459, 2004)* (Consider for similar populations as immunization recommendations.)	Immunization contraindicated if hypersensitivity to hen's eggs. Both amanfadine and rimantadine are about 60– 90% effective against influenza A. Both oseltamivir and zanamivir reported efficacious (82 & 84% respectively) in clinical trials *(JAMA 285 748, 2001; JID 186 1582, 2002)*. In families, rx of index case as well as contact cases was more effective than rx index case alone (p <0.01) *(JID 189 440, 2004)*

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function.

* From 2004 DRUG TOPICS RED BOOK, Medical Economics. Price is average wholesale price (AWP). **NB** = name brand; **G** = generic.

TABLE 14A (8)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Measles		
Children	No therapy or **vitamin A** 200 000 u po x2 days	Vitamin A ↓ severity of measles in one study *(NEJM 323 160, 1990)*, not in others
Adults	No rx or **ribavirin** IV (I) 20–35 mg/kg/d x7 d	↓ severity of illness in adults *(CID 20 454, 1994*
Metapneumovirus (HMPV)		
A paramyxovirus *(PIDJ 22 923 2003)* (solated from pts of all ages with illnesses ranging from mild bronchiolitis/bronchospasm to pneumonia All persons in the Netherlands had antibody to HMPV by age 5 yrs	**No proven antiviral therapy**	HMPV accounted for 2 3% of all respiratory viral isolates in Canada over the winter of 2000–2001 Similar to parainfluenza 2 3% adenovirus 3 4%, RSV 4 8% while influenza A & B was 20% *(JID 186 1330 2002)* Human metapneumovirus isolated from 6 2% of children with respiratory infections in Massachusetts *(JID 190 20 2004)* 12% in children with lower respiratory infections *(NEJM 350 443 2004)* & 21% of hospitalized children with URI in Norway *(PIDJ 23 436, 2004, JID 190 27, 2004*
Monkey pox (orthopox virus) *(see LnID 4 17 2004)*		
In 2003 72 pts contracted monkey pox from contact with ill prairie dogs Source likely imported Gambian giant rats *(MMWR 42 642, 2003)*	**No proven antiviral therapy** Cidofovir is active in vitro & in mouse model *(AAC 46 1329, 2002, Antiviral Res 57 13, 2003)*	Incubation period of 12 days then fever headache cough adenopathy & a vesicular papular rash that pustulates umbilicates & crusts on the head trunk & extremities
Norovirus (Norwalk-like virus or NLV)		
Caused 93% of outbreaks of non-bacterial gastroenteritis reported to CDC between 1997 & 2000 23 million cases of norovirus AGE annually in the U S *(JID 186 1 2002)* & account for 2/3 of all food-borne illnesses *(CID 38 748 2002)* Transmission is by contaminated food fecal-oral contact with contaminated surfaces or fomites Commonly causes outbreaks on cruise ships A new norovirus variant may account for ↑↑ number of cases in Europe *(Ln 363 682, 2004)*	**No antiviral therapy shown to be effective.** Elderly children, pts with co-morbid conditions may need volume repletion	Incubation period 12–48 hrs followed by sudden onset of nausea, vomiting & watery diarrhea lasting 12–60 hours
Papillomaviruses Therapies generally unsatisfactory with limited efficacy, high recurrence rates & ↑ side-effects *(JAC 53 137 2004)*		
Anogantal Warts Condyloma acuminatum *[See CID 28(Suppl 1) S37 1999]* [NOTE Results of Pap smear should be available prior to rx **avoid rx in pregnant women**] *NOTE Recurrences common after all treatments*	See *CID 27 796, 1998, for consensus statement* [**Podofilox** (Condylox) 2x daily application with cotton swab for 3 days followed by 4 days without rx repeat cycle 4–6x as necessary] **OR** [25% **podophyllin** in tincture of benzoin (Podocon-25) apply once weekly for up to 6 wks wash after 1–4 hrs] if no regression after 4 weekly applications use alternate rx	Podofilox Local reactions—pain burning inflammation in 50% No systemic effects Efficacy in penile warts 74% vs placebo 8% Recurrences 55% vs 100% with placebo (Podocon-25 15 ml $32 40 Condylox 3 5 ml $56 64) Warts recur in 1/3 with either agent within 1st month after rx
	Interferon alfa-2b (Intron A) **alfe-n3** (Alteron N) 1 million units (0 1 ml) into lesion 3x/week x3 weeks	Painful dilute to 10 million units/1 ml Other concentrations are hypertonic *(CID 28 S537 1999)* Use when other rx fails esp in AIDS
	Cryotherapy or electrosurgery	
	Imiquimod (5% cream) Apply 3x/week prior to sleep remove 6–10 hrs later when awake Continue until cleared or max 16 wks	When applied 3x/wk overnight for up to 16 wks or until warts completely cured produced clearance rates of 52% vs 14% for controls *(AAC 42 789, 1998)* Cost of 1–4 wks rx $108–432 Imiquimod Local reactions—mild erythema 60%, erosion 30% *[AJM 102(5A) 34, 1997]*
Skin papillomas	**Topical α-lactalbumin. Oleic acid** (from human milk) applied daily for 3 wks	↓ lesion size & recurrence vs placebo (p <0 001) *(NEJM 350 2663, 2004)* Further studies warranted
Parvo B19 Virus (Erythrovirus B19) *See NEJM 350 586 2004*		
Uncomplicated or self-limited acute arthritis May be chronic in children	**No treatment recommended**	Bone marrow shows selective erythrocyte maturation arrest with giant pronormoblasts IgM antibody available for diagnosis Specialty Labs Santa Monica CA Parvo B19 also associated with respiratory distress syndrome *(CID 27 900 1998)* and myocarditis/myocardiopathy *(CID 28 1343, 1999)*
Acute profound anemia in utero in hemolytic anemia, in HIV	**IVIG** 0 4 gm/kg IV qd x5 d in immune def states with severe anemia has been reported successful	IVIG contains anti-parvo B19 antibody In pts with pre-existing hemolytic anemia parvo B19-induced bone marrow arrest can result in sudden severe anemia *See Am J Hematol 61 16 1999 for new suggestions on management*

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function
* From 2004 DRUG TOPICS RED BOOK, Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14A (9)

VIRUS/DISEASE	DRUG/DOSAGE	SIDE EFFECTS/COMMENTS
Papovavirus/Polyomavirus		
Progresalve multifocal leukoencephalopathy (PML)(JC virus) Usually in pts with advanced HIV disease & organ transplant *(CID 35 1081 2002)*	*See SANFORD GUIDE TO HIV/AIDS THERAPY* **HAART** ↑ survival (545 d vs 60 d p < 0 001) and either improved (50%) or stabilized (50%) neurological deficits in 12 pts *(AIDS 12 2467 1999)* Others less optimistic *(CID 28 1152, 1999)*	Cytarabine of no value in controlled trial *(NEJM 338 1345 1998)* Camptothecin a human topoisomerase I inhibitor was administered to a single pt with slowing of progression *(Ln 349 1366, 1997)* Use of cidofovir controversial *(Clin Micro Rev 16 569 2003)*
Polyomavirus-aaeociated nephropathy	**Due to BK virus** post renal transplant	Possible rx role for **cidofovir** *(JnID 3 611 2003*
Rabias *(see Table 20C pages 141 142 see Mayo Clin Proc 79 671, 2004)* Rabid dogs account for 50 000 cases/yr worldwide Most cases in the U S are cryptic I e no documented evidence of bite or contact with a rabid animal *(CID 35 738 2003)* 70% assoc with 2 rare bat species the *eastern pipistrella* in the southeast & the *silver-hair bat* in the northwest *(EID 9 151 2003)* These viruses appear to exhibit ↑ infectivity	**Mortality 100% with only survivors those who receive rabies vaccine before the onset of illness/symptoms** *(CID 36 61 2003)* Therapies that have failed in human cases after symptoms develpo include rabies vaccine rabies immunoglobulin rabies virus neutralizing antibody ribavirin alfa interferon & ketamine	Corticosteroids ↑ mortality rate and ↓ incubation in mice
Respiratory Syncytial Virus Major cause of morbidity in neonates/infants *(JID 180 41 1999)* ↑ recognition in adults 2–9% of pts >65 yrs of age with pneumonia requiring hospitalization are due to RSV *(JID 179 25 1999)*	Rapid dx by antigen detection on nasopharyngeal wash No rx proven to ↑ survival Various combinations of ribavirin RSV-IVIG & palivizumab have been used see *Comments (PIDJ 23 707, 2004 Pharmacother 24 932, 2004 Ped Drugs 6 177 2004)*	Ribavirin reported to ↓ fever and other symptoms and signs However in controlled studies **ribavirin had no beneficial effect** *(J Ped 128 422, 1996 AJRCCM 160 829 1999)* Still recommended by some authorities in immunocompromised children *(PID 19 253, 2000)* & still controversial *(PIDJ 22 589 2003)*
Prevantion (1) Children <24 mos old with bronchopulmonary dysplasia (BPD) requiring supplemental O_2 (2) Perhaps premature infants (<26 wks gestation) and <6 mos old at start of RSV season	**RSV immune globulin intravenous** (RSV IVIG) 100 mg/kg IV once monthly Nov through April (for northern hemisphere) 1st year of life for prematures Perhaps up to 60 months of age for pts with BPD **OR** **Palivizumab** 15 mg/kg IM q month Nov -April as above *(Scand J Inf Dis 33 323 2001)*	RSV IVIG very expensive—estimated cost per infusion $1 175 See consensus opinion for details *Ped Inf Dis J 15 1059, 1996 See Ln 354 847 1999 for updated review* Palivizumab reduced hospitalization rates for RSV in 1500 premature infants & children with chronic lung disease from 10 6% to 4 8% *(Pediatrics 102 531 1998)* Cost $3000–5000/yr
Rhinovirus (Colds) *See Ln 361 51 2003* Found in ½ of children with community-acquired pneumonia role in pathogenesis unclear *(CID 39 681, 2004)*	No antiviral rx indicated Symptomatic rx • ipratropium bromide nasal (2 sprays/nostril tid) • clemastine 1 34 mg 1–2 tab po bid–tid (OTC)	Sx relief ipratropium nasal spray ↓ rhinorrhea and sneezing vs placebo *(AnIM 125 89 1996)* Clemastine (an antihistamine) ↓ sneezing rhinorrhea but associated with dry nose mouth & throat in 6–19% *(CID 22 656 1996)* Zinc lozenges were ineffective *(CID 31 1202 2000)* Oral **pleconaril** given within 24 hrs of onset reduced duration (1 day) & severity of 'cold symptoms in DBPCT[1] (p < 001) *(CID 36 1523 2003)* A combination of intranasal interferon alfa-2b oral chlorpheniramine & ibuprofen ↓ symptom score by 33–73% vs placebo when started 24 hrs after intranasal rhinovirus *(JID 186 147 2002)* Ruprintrivir inhibits rhinovirus 3C protease & ↓ symptom scores nasal discharge weights & viral titers in a DBPCT[1] in 202 subjects with rhinovirus colds *(AAC 47 3907, 2003)* Echinacea didn t work *(CID 38 1367, 2004*
SARS-CoV *See page 104*		
Smallpox *(NEJM 346 1300 2002)*	Smallpox vaccine (if within 4 days of exposure) + cidofovir (dosage uncertain contact CDC 770-488-7100)	
Contact vaccinia *(JAMA 288 1901 2002)*	From vaccination Progressive vaccinia—vaccinia immune globulin may be of benefit To obtain immune globulin contact CDC 770-488-7100 *(CID 39 759 776 & 819 2004)*	
West Nile virus *See page 104*		

[1] **DBPCT** = Double blind placebo-controlled trial

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** name brand **G** generic

TABLE 14B: ANTIVIRAL DRUGS (Other Than Retroviral)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE/COST*	COMMENTS/ADVERSE EFFECTS
CMV *(See SANFORD GUIDE TO HIV/AIDS THERAPY)*		
Cidofovir (Vistide)	5 mg/kg IV q week x2 then q2 weeks (375 mg $888) Properly timed IV prehydration with normal saline and oral probenecid **must be used with each cidofovir infusion** *(see pkg insert for details)* Renal function (serum creatinine and urine protein) must be monitored prior to each dose *(see pkg insert for details)*	**Adverse effects: Nephrotoxicity;** dose-dependent proximal tubular injury (Fanconi like syndrome) proteinuria glycosuria bicarbonaturia phosphaturia polyuria (nephrogenic diabetic insipidus now reported *Ln 350 413 1997*) ↑ creatinine Concomitant saline prehydration probenecid extended dosing intervals allowed use 25% of pts dc IV cidofovir due to nephrotoxicity Other toxicities nausea 48% fever 31% alopecia 16% myalgia 16% probenecid hypersensitivity 16% neutropenia 29% No effect on hematocrit platelets LFTs **Comment** Recommended dosage frequency or infusion rate of cidofovir must not be exceeded Dose must be reduced or discontinued if changes in renal function occur during rx For ↑ of 0 3–0 4 mg/dl in serum creatinine cidofovir dose must be reduced from 5 to 3 mg/kg discontinue cidofovir if ↑ of 0 5 mg/dl above baseline or 3+ proteinuria develops (for 2+ proteinuria observe pts carefully and consider discontinuation)
Fomivirsen (Vitravene)	330 µg by direct intravitreal injection q2 wks x2 then q month (6 6 mg $4000)	This is an antisense drug approved for local treatment of CMV retinitis in AIDS pts who are intolerant of have a contraindication to or were unresponsive to other treatments for CMV It inhibits production of proteins responsible for regulation of viral gene expression essential for virulence **Adverse effects:** ocular inflammation (uveitis) iritis and vitreitis ↑ intraocular pressure abnormal vision anterior chamber inflammation and cataracts Do not give if pt had received IV or intravitreal cidofovir (Vistide) within last 2–4 wks may exaggerate ocular inflammation *(Priority Pharmacy 3 #8 Oct 30 1998)*
Foscarnet (Foscavir)	90 mg/kg q12h IV (induction) 90 mg/kg qd (maintenance) Dosage adjust with renal dysfunction *(see Table 17)* (6 gm $85)	**Adverse effects. Major clinical toxicity is renal impairment (1/3 of patients)** –↑ creatinine, proteinuria, nephrogenic diabetes insipidus ↓K ↓ Ca^{++} ↓ Mg^{++} Toxicity ↑ with other nephrotoxic drugs [amphotericin B, aminoglycosides or pentamidine (especially severe ↓ Ca^{++})] Adequate hydration may ↓ toxicity Other headache mild (100%) fatigue (100%) nausea (80%) fever (25%) CNS seizures Hematol ↓WBC ↓Hgb Hepatic liver function tests ↑ Neuropathy Penile ulcers
Ganciclovir (Cytovene)	IV 5 mg/kg q12h x14 days (induction) 5 mg/kg IV qd or 6 mg/kg 5x/wk (maintenance) Dosage adjust with renal dysfunction *(see Table 17)* (500 mg IV $39)	**Adverse effects:** Absolute neutrophil count dropped below 500/mm^3 in 15% thrombocytopenia 21% anemia 6% Fever 48% GI 50% nausea vomiting diarrhea abdominal pain 19% rash 10% Retinal detachment 11% (relationship to ganciclovir ?) Confusion headache psychiatric disturbances and seizures Neutropenia may respond to granulocyte colony stimulating factor (G-CSF or GM-CSF) Severe myelosuppression may be ↑ with coadministration of zidovudine or azathioprine 32% dc/interrupted rx principally for neutropenia
	Oral 1 0 gm tid with food (fatty meal) (500 mg cap $9)	Hematologic less frequent than with IV Granulocytopenia 18% anemia 12% thrombocytopenia 6% GI skin same as with IV Retinal detachment 8%
Ganciclovir (Vitrasert)	Intraocular implant (~$5000/device + cost of surgery)	**Adverse affects:** Late retinal detachment (7/30 eyes) Does not prevent CMV retinitis in good eye or visceral dissemination **Comment:** Replacement every 6 months recommended
Valganciclovir (Valcyte)	900 mg (two 450 mg tabs) po bid x21 d for induction followed by 900 mg po qd Take with food (450 mg cap $31 50 ~$1 890 for 60 caps)	A prodrug of ganciclovir with better bioavailability 60% with food **Adverse effects:** Similar to ganciclovir
Herpesvirus (non-CMV)		
Acyclovir (Zovirax or generic)	Doses *see Table 14A* 400 mg tab NB $2 G $0 70 IV 500 mg NB $46 Suspension 200 mg/5 ml 1 gm $7 Ointment 5% 15 gm $107	**po:** Generally well-tolerated with occ diarrhea vertigo arthralgia Less frequent rash fatigue insomnia fever menstrual abnormalities acne sore throat muscle cramps lymphadenopathy **IV:** Phlebitis caustic with vesicular lesions with IV infiltration CNS (1%) lethargy tremors confusion hallucinations delirium seizures coma *(CID 21 435 1995)* Improve 1–2 weeks after rx stopped Renal (5%) ↑ creatinine hematuria With high doses may crystallize in renal tubules → obstructive uropathy (rapid infusion dehydration renal insufficiency and ↑ dose ↑ risk) Adequate pre-hydration may prevent such nephrotoxicity Hepatic ↑ ALT AST Uncommon neutropenia *(CID 20 1557 1995)* rash diaphoresis hypotension headache nausea
Famciclovir (Famvir)	250 mg cap $4 500 mg cap $8	Metabolized to penciclovir **Adverse effects:** similar to acyclovir included headache nausea diarrhea and dizziness but incidence did not differ from placebo *(JAMA 276 47 1996)* May be taken without regard to meals Dose should be reduced if CrCl <60 ml/min *(see package insert & Table 14 page 108 & Table 17, page 135)*
Penciclovir (Denavir)	Topical 1% cream 1 5 gm $26	Apply to area of recurrence of herpes labialis with start of sx then q2h while awake x4 d Well tolerated
Trifluridine (Viroptic)	1 drop 1% solution q2h (max 9 drops/d) for max of 21 d (7 5 ml 1% solution $99)	Mild burning (5%) palpebral edema (3%) punctate keratopathy stromal edema

NOTE: All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function

* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14B (2)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE/COST*	COMMENTS/ADVERSE EFFECTS
Herpesvirus (non-CMV) *(continued)*		
Valacyclovir (Valtrex)	500 mg cap $4 52	An ester pro-drug of acyclovir that is well absorbed bioavailability 3–5x greater than acyclovir **Adverse effects** similar to acyclovir *(see JID 186 540 2002)* Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome reported in pts with advanced HIV disease and transplant recipients particularly in clinical trials at doses of 8 g/day
Hepatitis		
Adefovir dipivoxil (Hepsera)	10 mg po qd (with normal CrCl) 20–50 CrCl 10 mg q48h 10–19 CrCl 10 mg q72h Hemodialysis 10 mg q7 days following dialysis Each tab contains 10 mg ($19)	Adefovir dipivoxil is a diester prodrug of the active moiety adefovir It is an acyclic nucleotide analog with activity against hepatitis B (HBV) at 0 2–2 5 mM (IC_{50}) Peak plasma concentration after 10 mg po was 18 4 ± 6 26 ng/ml, 1–4 hrs after dose Terminal elimination t½ was 7 48 ± 1 65 hrs Primarily renal excretion—adjust dose No food interactions Remarkably few side effects Nephrotoxicity found in early studies with 30 mg/d not yet reported at 10 mg/d Monitor renal function, esp with pts with pre-existing or other risks for renal impairment Lactic acidosis reported with nucleoside analogs esp in women Pregnancy Category C Hepatitis may exacerbate when rx dc 6–25% of pts developed ALT ↑ 10x normal within 12 wks usually responds to re-treatment or self-limited, but hepatic decomposition has occurred
Interferon alfa is available as alfa-2a (Roferon-A), alfa-2b (Intron-A)	3 million units (Roteron $37, Intron $39 Infergen 9 µg $48)	**Adverse effects** Flu like syndrome is common esp during 1st week of rx fever 98% fatigue 89% myalgia 73% headache 71% GI anorexia 46% diarrhea 29% CNS dizziness 21% Rash 18% later profound fatigue & psychiatric symptoms in up to ½ of pts *(J Clin Psych 64 708 2003)* (depression, anxiety emotional lability and agitation) alopecia ↑ TSH autoimmune thyroid disorders with hypo- or hyperthyroidism Hematol ↓ WBC 49% ↓ Hgb 27% ↓ platelets 35% Consider prophylactic antidepressant in pts with history Acute reversible hearing loss and/or tinnitus in up to 1/3 *(Ln 343 1134 1994)* Optic neuropathy (retinal hemorrhage cotton wool spots ↓ in color vision) reported *(AIDS 18 1805 2004)* Side-effects ↑ with ↑ doses and dose reduction necessary in up to 46% receiving chronic rx for HBV
PEG Interferon alfa-2b (PEG-Intron)	0 5-1 5 µg/kg sc q wk (120 µg $391)	
Pegylated-40k Interferon alfa-2a (Pegasys)	180 µg sc q wk x48 wks (180 µg $367)	Attachment of INF to polyethylene glycol (PEG) prolongs half-life and allows weekly dosing Better efficacy data with similar adverse effects profile compared to regular formulation
Lamivudine (3TC) (Epivir-HBV)	**Adverse effects** *See Table 14D page 121* NOTE 100 mg po qd x1 yr for hepatitis B (100 mg tab $7)	
Ribavirin–interferon alfa-2b combination pack (Rebetron)	Combination kit contains 2 wk supply of INF and 42 70 or 84 caps of 200 mg ribavirin **Dose** INF 3 million U sc tiw AND ribavirin 400 mg po q a m + 600 mg po q p m (<75 kg) or 600 mg po bid (>75 kg) Rebetron (1000 mg/d ribavirin dose pack) ($9652/24 wk course)	Side-effects common with flu-like symptoms (>50%) *see interferon alfa above* Hemolytic anemia common (mean reduction in Hgb 3 gm/dl) but usually responds to ↓ ribavirin dosage *(see package insert)* **Severe psychiatric effects, esp. depression, most common (23–36%) reason for discontinuation of rx. Suicidal behavior reported** Hyper & hypothyroidism alopecia (30%) & pulmonary disease reported *(Mayo Clin Proc 74 367 1999)* **Since ribavirin is teratogenic, drug must not be used during pregnancy or within 6 months of pregnancy** Also should not be used in pts with endstage renal failure severe heart disease or hemoglobinopathies ARDS reported *(Chest 124 406 2003)*

Dose changes	**Ribavirin**	**Interferon**
Hgb <10	↓ to 200 mg q a m 400 mg q p m	No change
<8 5	DC	DC
WBC <1500	No change	↓ to 1 5 mIU sc 3x/wk
<1000	DC	DC
Abs PMNs <750	No change	↓ to 1 5 mIU sc 3x/wk
<500	DC	DC
Platelets <50 000	No change	↓ to 1 5 mIU sc 3x/wk
<25 000	DC	DC

Response of immune complex renal disease *AJM 106 347 1999*

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function
* From 2004 DRUG TOPICS RED BOOK Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14B (3)

DRUG NAME(S) GENERIC (TRADE)	DOSAGE/ROUTE/COST*	COMMENTS/ADVERSE EFFECTS
Hepatitis *(continued)*		
Ribavirin (Rebetol)	For use with an interferon for hepatitis C & was unbundled from the combination Rebetron *(see above)* mostly for use with the pegylated interferons (alfa 2a & 2b) Available as 200 mg capsules Dose <75 kg BW = 2 caps in a m & 3 caps in p m >75 kg BW 3 caps in a m & 3 caps in p m Cost 200 mg $10	Side effects as above esp hemolytic anemia (during 1st 1–2 wks of rx) with hemoglobin ↓ of 3–4 gm Should not be used with CrCl <50 ml/min & cautiously with cardiac disease
Influenza A		
Amantadine (Symmetrel) or Rimantadine (Flumadine)	Amantadine and rimantadine doses are the same (rimantadine approved only for prophylaxis in children not treatment) Amantadine 100 mg po bid >65 y o 100 mg po qd G 100 mg cap $0 50 100 mg/10 ml soln $1 80 Rimantadine 100 mg tab/syrup $2	**Side-effects/toxicity:** CNS (nervousness anxiety difficulty concentrating and lightheadedness) Symptoms occurred in 6% on rimantadine vs 14% on amantadine They usually ↓ after 1st week and disappear when drug dc GI (nausea anorexia) Some serious side-effects—delirium hallucinations and seizures—are associated with high plasma drug levels resulting from renal insufficiency esp in older pts those with prior seizure disorders or psychiatric disorders In pts with impaired renal function dosage of both drugs should be reduced (amantadine creatinine clearance <50 ml/min rimantadine CrCl <10 ml/min) *see package inserts and Table 17, pages 135 & 136* Both drugs teratogenic in animals and contraindicated during pregnancy *(Med Lett 39 72, 1997)*
Influenza A and B—For both drugs, initiate within 48 hrs of symptom onset		
Zanamivir (Relenza) For pts ≥12 yrs of age	2 inhalations (2 x 5 mg) bid x5 d Powder is inhaled using specially designed breath-activated device Each medication-containing blister contains 5 mg of zanamivir $57/course	Active by inhalation against neuraminidase of both influenza A and B and inhibits release of virus from epithelial cells of respiratory tract Approx 4–17% of inhaled dose absorbed into plasma Excreted by kidney but with low absorption dose reduction not necessary in renal impairment Minimal side-effects <3% cough sinusitis diarrhea nausea and vomiting **Reports of respiratory adverse events in pts with or without h/o airways disease, should be avoided in pts with respiratory disease.**
Oseltamivir (Tamiflu)	75 mg po bid for treatment [pediatric suspension (12 mg/ml) approved for treatment not prevention in children age 1–12 at dose of 2 mg/kg (up to 75 mg total) bid x5 d] For prevention 75 mg po qd for duration of peak of flu epidemic $38/5 day course	Well absorbed (80% bioavailable) from GI tract as ethyl ester of active compound GS 4071 T½ 6–10 hrs excreted unchanged by kidney Adverse effects in 15% include diarrhea 1 6% nausea 0 5% vomiting headache *(J Am Ger Soc 50 608, 2002)* Nausea ↓ with food Also available as 12 mg/ml oral suspension
Respiratory Syncytial Virus (RSV) and other		
Palivizumab (Synagis) *(See Med Lett 41 1, 1999)* Used only for prevention of RSV infection in high-risk children *(Ped 102 1211, 1998)*	15 mg/kg IM q month 100 mg vial (for 1 injection) $1312	A monoclonal antibody directed against the F glycoprotein on surface of virus side-effects are nominal occ ↑ ALT *(JID 176 1215, 1997)*
Ribavirin (Virazole)	1 1 gm/day (6 gm vial for inhalation $1374)	**Ribavirin side-effects:** Anemia rash conjunctivitis Read package insert Avoid procedures that lead to drug precipitation in ventilator tubing with subsequent dysfunction Significant teratogenicity in animals **Contraindicated in pregnant women and partners** Pregnant health care workers should avoid direct care of pts receiving aerosolized ribavirin
RSV IV immunoglobulin (IG) (RespiGam)	100 mg/kg IV q month (50 ml $1030)	RespiGam side effects rare but include fatal anaphylaxis pruritus rash wheezing, fever joint pain
Warts *(See CID 28 S37, 1999)*		
Interferon alfa-2b or alfa-n3	Apply 1 million units into lesion	Interferon alfa-2b 3 million units/0 5 ml, interferon alfa-n3 5 mU/1 ml Cost $10
Podofilox (Condylox)	3 5 ml for topical application, $130	**Side-effects:** Local reactions—pain burning, inflammation in 50% No systemic effects
Imiquimod (Aldara)	Cream applied 3x/week to maximum of 16 wks 250 mg packets $15	Mild erythema erosions, itching and burning

NOTE All dosage recommendations are for adults (unless otherwise indicated) and assume normal renal function
* From 2004 DRUG TOPICS RED BOOK, Medical Economics Price is average wholesale price (AWP) **NB** = name brand **G** = generic

TABLE 14C: ANTIRETRDVIRAL THERAPY IN ADULTS

(See the 2004 SANFORD GUIDE TO HIV/AIDS THERAPY Table 6 for additional information regarding treatment and complications of antiretroviral agents)

In 2004 several guidelines and recommendations for the treatment of individuals infected with HIV-1 were updated Among these were DHHS guidelines for treatment of infected adults and adolescents guidelines for the use of antiretroviral therapy (ART) in pediatrics and recommendations for ART in pregnant women All of these documents are available online at *www aidsinfo nih gov* New treatment recommendations by the International AIDS Society–USA Panel were published mid year *(JAMA 292 251, 2004)* as were guidelines for primary care management of HIV-infected persons provided by the HIV Medicine Association of the IDSA *(CID 39 609, 2004)*

A. When to start therapy? *(www aidsinfo nih gov)*

• HIV Symptoms	CD4 cells/µl	Start Treatment	Comment
Yes	Any	Yes	
No	<200	Yes	
No	>200–≤350	Offer *(see Comment)*	Risk for progression to AIDS also depends on viral load consider on individual basis
No	>350	No *(see Comment)*	Maybe if CD4 decreasing rapidly and/or viral load >100 000 copies/ml

- Acute retroviral syndrome—*See page 117 section C*

B. Suggested Initial Therapy Regimens for Untreated Chronic HIV Infection *(For pregnancy, see below and Table 8 of the Sanford Guide to HIV/AIDS Therapy 2004)*

1. Preferred Regimens

	Regimen	Capsule (pill size, mg)	Daily Regiman	No. pills/ day	Cost/month (AWP)[1]	Comment
a	**(Zidovudine + Lamivudine)+ Efavirenz‡**	(300 + 150) + 600	**(Combination—Combivir** 1 tab po bid) + 1 tab po qd hs, empty stomach[2]	3	$1090	Good efficacy, low pill burden, low AE profile **If rx stopped, dc efavirenz 1–2 wks before Combivir** *(for explanation, see footnote page 118*
b	**(Tenofovir + Emtricitabine)+ Efavirenz‡**	(300 + 200) + 600	**(Combination—Truvada** 1 tab po qd) + 1 tab po qd	2	$1168	Tenofovir emerging reports of renal toxicity Do not use efavirenz 1st trimester of pregnancy
c	**(Zidovudine + Lamivudine) + Lopinavir/ Ritonavir**	(300 + 150) + 133 3/33 3	**(Combination—Combivir** 1 tab po bid) + 3 tabs po bid with food	8	$1362	Good virologic efficacy and durable effect Tolerable AEs Possible elevated triglycerides. ↓ accumulation of resistance mutations than nelfinavir regimen *(NEJM 346 2039, 2002).*
2.	**Alternative Regimens**					
a	**Didanosine EC + Lamivudine* + Efavirenz‡**	400 + 300 + 600	1 cap po daily hs fasting + 1 tab po daily + 1 tab po daily hs empty stomach[2]	3	$1037	Low pill burden Efficacy and durability under study Potential didanosine AEs **didanosine dosage shown for ≥60 kg**
b	**Fosemprenavir + Ritonavir + (Zidovudine + Lamivudine)**	700 + 100 + (300 + 150)	1 tab po bid fed or fasting 1 tab po bid fed or fasting **(Combination—Combivir** 1 tab po bid)	6		Lower pill burden with fosamprenavir as compared to amprenavir
c	**(Zidovudine + Lamivudine)+ Nelfinavir**	(300 + 150) + 625	**(Combination—Combivir** 1 tab po bid) + 2 tabs po bid with food	6	NA	Good efficacy Nelfinavir associated diarrhea in 20% Nelfinavir contraindicated with drugs highly dependent on CYP3A4 elimination where ↑ levels may cause life threatening toxicity
3.	**Triple nucleoside or nucleoside/nucleotide regimen: Due to interior virologic activity, use only when preferred or alternative regimen not possible.**					
a	**(Zidovudine + Lamivudine + Abacavir)**	(300 + 150 + 300)	**(Combination—Trizivir** 1 tab po bid) Avoid alcohol	2	$1065	Reduced efficacy as compared to preferred & alternative regimens Potential serious abacavir AEs
4.	**During pregnancy. Expert consultation mandatory**					
a	**(Zidovudine + Lamivudine) + Navirapine**	(300 + 150) + 200	**(Combination—Combivir** 1 tab po bid) + 1 tab po bid fed or fasting [after 14-day lead in period of 1 tab po daily]	4	$1040	Monitor hepatic-associated enzymes 11% of women with CD4 >250/mm³ had symptomatic events **See Black box warnings** *(page 121)* Timing of treatment initiation and choice of drugs must be individualized certain drugs contraindicated *See www aidsinfo nih gov* for details alternative NRTIs and possible PI based regimens Resistance testing should be strongly considered For regimens to prevent mother-child transmission *see www aidsinfo nih gov*

[1] **AWP** – average wholesale price

[2] Food may ↑ serum concentration which can lead to ↑ in the risk of adverse events

C. Suggested Regimen for Acute Primary HIV Infection (mono-like syndroma)

Regimen	Capsule (pill size, mg)	Daily Regimen	No. pills/day	Cost/month (AWP)[1]	Comment
(Zidovudine + Lamivudine) + **Efavirenz‡**	**Zidovudine** 300 mg + **Lamivudina** 150 mg + 600 mg tab	(**Combination—Combivir** 1 tab po bid) + 1 tab po hs empty stomach[2]	3	$1090	Adherence to rx is crucial Check genotype Treatment considered optional because benefits not yet defined Duration of therapy is unknown *(see http //aidsinfo nih gov)*

* Can substitute emtricitabine (FTC) 200 mg po daily for lamivudine
‡ Avoid efavirenz in pregnancy, in women who wish to conceive, or in women not using effective contraception

D. Some Antiretroviral Therapies Should NOT Be Offered; *see 2004 Sanford Guide to HIV/AIDS Therapy, Table 6, for details*

E. Selected Characteristics of Antiretroviral Drugs

1. Selected Characteristics of Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs)*

Generic/Trade Name	Pharmaceutical Prep. (AWP)[1]	Usual Adult Dosage	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	Elimination	Major Adverse Events/Comments
Abacavir (Ziagen)	300 mg tabs or 20 mg/ml oral solution ($408/month)	300 mg po bid or 600 mg po qd Food OK	83	1 5	20	Liver metab , renal excretion of metabolites, 82%	Hypersensitivity reaction fever, rash, N/V, diarrhea, abdominal pain, respiratory symptoms (Severe reactions may be ↑ with 600 mg dose) **Do not rechallenge!** Report to 800-270-0425 Lactic acidosis with hepatic steatosis
Didenosine (ddI Videx or Videx EC)	25 50 100 150 200 mg chewable tabs 100 167 250 mg powder for oral solution 125 200 250 400 enteric-coated caps ($313/month Videx EC)	≥60 kg Usually 400 mg enteric-coated po qd ½ hr before or 2 hrs after meal **Do not crush** <60 kg 250 mg EC po qd *See Comment*	30–40	1 6	25–40	Renal excretion 50%	Pancreatitis peripheral neuropathy lactic acidosis & hepatic steatosis (rare but life-threatening) **Reduce dose to 250 mg EC qd if used with tenofovir.**
Emtricitabine (FTC, Emtriva)	200 mg caps ($290/month)	200 mg po qd No significant effect of food	50–95% in animal studies	Approx 10	>20	Renal excretion 86% minor biotransformation, 14% excretion in feces	Well tolerated headache 20%, nausea, vomiting & diarrhea occasionally, skin rash rarely Skin hyperpigmentation Potential for lactic acidosis with hepatic steatosis Differs only slightly in structure from lamivudine (5-fluoro substitution) Also active vs hepatitis B, exacerbation of Hep B reported in pts after DC of FTC
Emtricitabine/tenofovir disoproxil fumarate (Truvada)	Film-coated tabs FTC 200 mg + TDF 300 mg	1 tab po qd for CrCl ≥50 ml/min Food OK	92/25	10/17	—	Primarily renal/renal	*See Comments for individual agents*
Lamivudine (3TC; Epivir)	150, 300 mg tabs, 10 mg/ml oral solution ($303/month)	150 mg po bid or 300 mg po qd Food OK	86	5–7	16	Renal excretion, minimal metabolism	Safest of NRTIs Rare life-threatening lactic acidosis/hepatic steatosis Potential exacerbation of Hep B after DC
Lamivudine/abacavir (Epzicom)	Film-coated tabs 3TC 300 mg + **abacavir 600 mg**	1 tab po qd for CrCl ≥50 ml/min Food OK	86/86	5–7/1 5	16/20	Primarily renal/ metabolism	*See Comments for individual agents* **Note abacavir hypersensitivity Black Box warninga** (severe reactions may be ↑ with 600 mg dose)

[1] **AWP** = average wholesale price
[2] Food may ↑ serum concentration which can lead to ↑ in the risk of adverse events

TABLE 14C (3)

1. **Selected Characteristics of Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs)*** *(continued)*

Generic/Trade Name	Pharmaceutical Prep. (AWP)[1]	Usual Adult Dosage	% Absorbed, po	Serum T½, hrs	Intracellular T½, hrs	Elimination	Major Adverse Events/Comments
Lamivudine/zidovudine (Combivir)	Film-coated tabs 3TC 150 mg + ZDV 300 mg	1 tab po bid for CrCl ≥50 ml/min Food OK	86/64	5–7/0 5–3	—	Primarily renal/ metabolism with renal excretion of glucuronide	*See Comments for individual agents*
Stavudine (d4T, Zerit, Zerit XR)	15, 20, 30, 40 mg capsules or 75, 100 mg extended-release (XR) caps, 1 mg/ml oral solution ($347/month 40 mg caps)	≥60 kg 40 mg cap bid or 100 mg XR cap qd[4,5] <60 kg 30 mg cap bid or 75 mg XR cap qd[4,5] Food OK	86	1	3 5	Renal excretion, 50%	**Highest incidence of lipoatrophy, hyperlipidamia, & lactic acidosis of all NRTIs** Pancreatitis XR formulation FDA-approved, but not yet available (Oct 2004).
Tenofovir disoproxil fumarate (Viread)—a nucleotide	300 mg tabs ($432/month)	CrCl ≥50 ml/min 300 mg qd Food OK high-fat meal ↑ absorption	39	17	10–50	Renal excretion	Asthenia headache N/V Potential lactic acidosis/hepatic steatosis (rare reports with combinations) Cases of renal dysfunction reported If combined with didanosine lower didanosine dose to 250 mg EC qd
Zalcitabine (ddC; Hivid)	0 375, 0 75 tabs ($246/month)	0 75 mg po tid Food OK	85	1.2	3	Renal excretion, 70%	Peripheral neuropathy, stomatitis, rarely life-threatening lactic acidosis, pancreatitis
Zidovudine (ZDV AZT Retrovir)	100 mg caps 300 mg tabs 10 mg/ml IV solution 10 mg/ml oral solution ($355/month)	300 mg po bid Food OK	60	1 1	3	Metabolized to glucuronide & excreted in urine	Bone marrow suppression GI intolerance headache, insomnia weakness rarely lactic acidosis

*** All agents have Black Box warning:** risk of lactic acidosis/hepatic steatosis Also labels note risk of fat redistribution/accumulation with ARV rx

2. **Selected Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**

Generic/Trade Name	Pharmaceutical Prep. (AWP)[1]	Usual Adult Dosage	% Absorbed, po	Serum T½, hrs	Elimination	Major Adverse Events/Comments
Delavirdine (Rescriptor)	100, 200 mg tabs ($316/month)	400 mg po tid Food OK	85	5 8	Cytochroma P450 (3A inhibitor) 51% excreted in urine (<5% unchanged), 44% in feces	Rash severe enough to dc use of drug in 4 3% ↑ SGOT/SGPT, headaches
Efavirenz (Sustiva) *See footnote*[2]	50 100 200 mg capsules, 600 mg tablet ($432/month)	600 mg tab po hs without food[3]	42	40–55 *See footnote*[3]	Cytochrome P450 (3A mixed inducer/ inhibitor) 14–34% of dose excreted in urine as glucuronidated metabolites 16–61% in feces	Rash severe enough to dc use of drug in 1 7% High frequency of diverse CNS AEs somnolence dreams contusion agitation false positive cannabinoid test Fetal mal formations in monkeys
Nevirapine (Viramune)	200 mg tabs, 50 mg/5 ml oral suspension ($382/month)	200 mg po qd x14 d & then 200 mg po bid *(see Comments)* Food OK	>90	25–30	Cytochroma P450 (3A) inducer, 80% of dose excreted in urine as glucuronidated metabolites, 10% in feces	Follow dose-escalation protocol **Black Box warning** re fatal hypersensitivity, skin reactions, & hepatotoxicity Women with CD4 >250 esp vulnerable, including pregnant women Don t restart if any suspicion of such reactions Rash severe enough to dc use of drug in 7%, severe or life-threatening in 2%

[1] **AWP** = average wholesale price
[2] **Efavirenz:** Very long tissue half-life If efavirenz to be discontinued stop efavirenz 1–2 wks before stopping companion drugs If all drugs stopped concomitantly risk of developing efavirenz resistance as after 1–2 days only efavirenz in blood and/or tissue
[3] Food may ↑ serum concentration which can lead to ↑ in the risk of adverse events

3. Selected Characteristics of Protease Inhibitors (PIs)*

Generic/Trade Name	Pharmaceutical Prep. (AWP)[1]	Usual Adult Dosage	% Absorbed, po	Serum T½, hrs	Elimination	Major Adverse Events/Comments
Ampranavir (Agenerase)	50 150 mg capsules *(see Comment)* 15 mg/ml oral solution (For oral solution dosage see package insert or PDR) ($736/month)	1200 mg (Eight 150 mg capsules) po bid OR With ritonavir [600 mg amprenavir (4 caps) + ritonavir 100 mg] po bid OR (1200 mg amprenavir caps + 200 mg ritonavir) po qd	No data Food OK avoid high-fat meal	7 1–10 6	Cytochrome P450 (3A4 inhibitor)	Nausea/vomiting diarrhea rash oral paresthesias ↑ SGOT/ SGPT Contains sulfa moiety **Black Box warning:** Oral solution contains propylene glycol do not use in pregnancy children <4 y/o, renal/hepatic failure with disulfiram or metronidazole Use oral solution only when essential **Sale of 150 mg caps in U.S. to be discontinued after 2004.**
Atazanavir (Reyataz)	100, 150, 200 mg capsules ($788/month)	400 mg qd with food (exception is atazanavir 300 mg qd + ritonavir 100 mg qd when combined with efavirenz 600 mg qd or TDF 300 mg qd) Take with food 2 hrs pre or 1 hr post buffered ddI Dosage adjustment in hepatic insufficiency Child-Pugh Class B—300 mg qd, Child-Pugh Class C—avoid *(See Comments)*	Good oral bioavailability, food enhances bioavailability & ↓ pharmacokinetic variability	Approx 7	Cytochrome P450 (3A4 inhibitor) & UGT1A1 inhibitor, 13% excreted in urine (7% unchanged), 79% excreted in feces (20% unchanged)	No ↑ lipids in available studies Asymptomatic unconjugated hyperbilirubinemia common Headache rash GI symptoms **Prolongation of PR interval (1st degree AV block) reported.** Caution in pre-existing conduction system disease **Efavirenz & tenofovir ↓ atazanavir exposure: use atazanavir/ritonavir regimen; also, atazanavir ↑ tenofovir concentrations—watch for adverse events** *(see www.fda.gov/oashi/aids/new.html)*
Fosamprenavir (Lexiva)	700 mg tablet	1400 mg (two 700 mg tabs) po bid OR With ritonavir [1400 mg fosamprenavir (2 tabs) + ritonavir 200 mg] po qd OR [700 mg fosamprenavir (1 tab) + ritonavir 100 mg] po bid	Bioavailability not established Food OK	7 7	Cytochrome P450 (3A4 substrate inhibitor, inducer)	Amprenavir prodrug *(See amprenavir adverse events.)* Once daily regimen (1) not recommended for PI-experienced pts (2) additional ritonavir needed if given with efavirenz *(see label)*
Indinavir (Crixivan)	100, 200, 333, 400 mg capsules ($546/month)	Two 400 mg caps (800 mg) po q8h Without food or with light meal Can take with enteric-coated Videx *[If taken with ritonavir (e.g., 800 mg indinavir + 100 mg ritonavir po bid), no food restrictions]*	65	1.2–2	Cytochrome P450 (3A4 inhibitor)	**Nephrolithiasis**, nausea, inconsequential ↑ of indirect bilirubin, ↑ SGOT/SGPT, headache asthenia, blurred vision, metallic taste, hemolysis ↑ urine WBC (>100/hpf) has been assoc. with nephritis/medullary calcification, cortical atrophy
Lopinavir + ritonavir (Kaletra) Can be kept at room temperature x2 mos	(133.3 mg lopinavir + 33.3 mg ritonavir) capsules Oral solution (80 mg lopinavir + 20 mg ritonavir)/ml Refrigerate ($703/month)	(400 mg lopinavir + 100 mg ritonavir)—3 caps po bid with food Higher dose of 4 caps (533 mg lopinavir + 133 mg ritonavir) po bid recommended when used with efavirenz nevirapine, amprenavir, nelfinavir [Dose adjustment in concomitant drugs may be necessary, *see Table 22B & C, page 149*]	Take with food for ↑ absorption	5–6	Cytochrome P450 (3A4 inhibitor)	Nausea/vomiting/diarrhea asthenia ↑ SGOT/ SGPT Oral solution 42% alcohol

[1] **AWP** = average wholesale price

TABLE 14C (5)

3. Selected Characteristics of Protease Inhibitors (PIs)* *(continued)*

Generic/Trade Name	Pharmaceutical Prep. (AWP)[1]	Usual Adult Dosage	% Absorbed, po	Serum T½, hrs	Elimination	Major Adverse Events/Comments
Nelfinavir (Viracept)	625, 250 mg tabs, 50 mg/gm oral powder ($757/month)	2 625 mg tabs (1250 mg) po bid, with food, or 5 250 mg tabs (1250 mg) po bid	20–80	3 5–5	Cytochrome P450 (3A4 inhibitor)	Diarrhea Coadministration of drugs with life-threatening toxicities & which are cleared by CYP34A is contraindicated
Ritonavir (Norvir) Room temperature x1 mo OK Many drug interactions—*see Table 22A–C pages 146 & 149*	100 mg capsules 600 mg/7 5 ml solution Refrigerate caps but not solution ($772/month)	Full dose 6 caps (600 mg) po q12h with food Escalate to full dose 300 mg bid x2 d , 400 mg bid x3 d , 500 mg bid x7 d then full dose "Booster drug"—*see Comment*	Approx 65	3–5	Cytochrome P450 Potent 3A4 inhibitor	Nausea/vomiting/diarrhea extremity & circumoral paresthesias hepatitis pancreatitis taste perversion ↑ CPK & uric acid **Used to enhenca pharmacokinetics of other PIa, ueing lower ritonevir doses.**
Saquinevir (Invireae) hard gel caps + ritonavir	Saquinavir 200 mg caps; ritonavir 100 mg caps ($1230/month)	5 caps saquinavir (1000 mg) + 1 cap ritonavir (100 mg) po bid with food	Erratic, 4 (saquinavir alone)	1–2	Cytochrome P450 (3A4 inhibitor)	Nausea, diarrhea, headache, ↑ SGOT/SGPT
Saquinavir (Fortovaae) aoftgel capa	200 mg capsules Retrigerate (can be kept at room temperature x3 mos) ($720/month)	6 caps (1200 mg) po tid with food OR 5 caps saquinavir (1000 mg) + 1 cap ritonavir (100 mg) po bid with tood	Not known	1–2	Cytochrome P450 (3A4 inhibitor)	Nausea diarrhea abdominal pain headache, ↑ SGOT/SGPT
Tipranevir[NDA] (Texega)		500 mg with ritonavir 200 mg bid in Phase III studies	30% in animal studies, ↑ AUC & peak plasma conc. in presence of food & if combined with ritonavir		Cytochrome P450 (3A4 mixed inducer/inhibitor)	Nausea/vomiting, diarrhea, abdominal pain Limited availability for compassionate use if CD4 count <100, call 800-632-2464

*** All PIa:** Glucose metabolism new diabetes mellitus or deterioration of glucose control, fat redistribution possible hemophilia bleeding hypertriglyceridemia or hypercholesterolemia

4. Selected Characteristics of Fusion Inhibitors

Generic/Trede Name	Pharmaceutical Prep. (AWP)[1]	Uaual Adult Dosage	% Absorbed	Serum T½, hrs	Elimination	Major Adverse Events/Commants
Enfuvirtido (T20 Fuzeon)	Single-use vials of 90 mg/ml when reconstituted Vials should be stored at room temperature Reconstituted vials can be refrigerated for 24 hrs only (~$20 000/year)	90 mg (1 ml) sc bid	84 3 ± 15 5	3 8 ± 0 6	Catabolism to its constituent amino acids with subsequent recycling of the amino acids in the body pool Elimination pathway(s) have not been performed in humans Does not alter the metabolism of CYP3A4 CYP2D6 CYP1A2 CYP2C19 or CYP2E1 substrates	Local reaction site reactions 98% <3% DC erythema/induration ~80–90% nodules/cysts ~80% Hypersensitivity reactions reported—do not restart if occur Including background regimens, peripheral neuropathy 8 9% insomnia 11 3% ↓ appetite 6 3% myalgia 5% lymphadenopathy 2 3% eosinophilia ~10% ↑ incidence of bacterial pneumonias Alone offers little benefit to a failing regimen *(NEJM 348 2249, 2003)*

[1] **AWP** average wholesale price

TABLE 14D: ANTIRETROVIRAL DRUGS AND ADVERSE EFFECTS *www.aidsinfo.nih.gov—accessed Sept. 2004*

DRUG NAME(S): GENERIC (TRADE)	ADVERSE EFFECTS
Nucleoside Reverse Transcriptase Inhibitors (NRTI)[1]	
Abacavir (Ziagen)	**Most common:** Headache 7–13% nausea 7–19%, diarrhea 7%, malaise **Most significant: Black Box warning—Hypersensitivity reaction** in 5% with malaise, fever, GI upset, rash, lethargy, & respiratory symptoms most commonly reported, myalgia, arthralgia, edema, paresthesia less commonly reported **Rechallenge contraindicated; may be life-threatening.**
Didanosine (ddI) (Videx)	**Most common:** Diarrhea 28% nausea 6% rash 9% headache 7% fever 12% hyperuricemia 2% **Most significant: Pancreatitis 1–9% Black Box warning—Cases of fatal and nonfatal pancreatitis** have occurred in pts receiving ddI especially when used in combination with d4T or d4T + hydroxyurea Peripheral neuropathy in 20%, 12% required dose reduction
Emtricitabine (FTC, Emtriva)	**Most common:** Headache 20%, diarrhea, nausea, rash, skin hyperpigmentation **Most significant:** Potential for lactic acidosis (as with other NRTIs), exacerbation of hepatitis B on stopping drug
Lamivudine (3TC) (Epivir)	Well tolerated Headache 35% nausea 33% diarrhea 18% abdominal pain 9% insomnia 11% (in combination with ZDV) Pancreatitis more common in pediatrics (15%) **Black Box warning:** Make sure to use HIV dosage not Hep B dosage
Stavudine (d4T) (Zerit)	**Most common:** Diarrhea, nausea, vomiting, headache **Most significant: Peripheral neuropathy** 15–20% Pancreatitis 1% Appears to produce lactic acidosis more commonly than other NRTIs **Black Box warning—Fatal & nonfatal pancreatitis with d4T + ddI ± hydroxyurea. Fatal lactic acidosis/steatosis in pregnant women receiving d4T + ddI.** Motor weakness in the setting of lactic acidosis mimicking the clinical presentation of Guillain-Barre syndrome including respiratory failure) (rare)
Zalcitabine (ddC) (Hivid)	**Most common:** Oral ulcers 13% rash 8% **Most significant: Black Box warning—**Pancreatitis <1% **peripheral neuropathy** 22–35% Severe continuous pain slowly reversible when ddC is discontinued ↑ risk with diabetes mellitus **Hepatic failure in pts with Hep B.**
Zidovudine (ZDV, AZT) (Retrovir)	**Most common:** Nausea 50%, anorexia 20%, vomiting 17%. **headache 62%** malaise 53% Also reported asthenia, insomnia, myalgias, nail pigmentation **Macrocytosis** expected with all dosage regimens **Most significant: Black Box warning—hematologic toxicity, myopathy. Anemia** (<8 gm/dL 1%), granulocytopenia (<750 1–8%) Anemia may respond to epoetin alfa if endogenous serum erythropoietin levels are <500 mU/ml
Nucleotide Reverse Transcriptase Inhibitor (NtRTI)[1]	
Tenofovir (Viread)	**Most common:** Nausea 11% diarrhea 9% vomiting 5% flatulence 4% (generally well tolerated) **Most significant: Black Box warning—Severe exacerbations of Hep B in co-infected pts. DC tenofovir. Not indicated for rx of chronic Hep B.** Reports of Fanconi syndrome & renal injury induced by tenofovir (*Intl J Kidney Dis 40:1331, 2002; CID 37:e174, 2003*)
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)	
Delavirdine (Rescriptor)	**Most common:** Nausea, diarrhea, vomiting, headache **Most significant: Skin rash** has occurred in 18%, can continue or restart drug in most cases Stevens-Johnson syndrome and erythema multiforme have been reported rarely ↑ in liver enzymes in <5% of patients
Efavirenz (Sustiva)	**Most common: CNS side-effects 52%;** symptoms include dizziness insomnia, somnolence impaired concentration psychiatric sx and abnormal dreams symptoms are worse after 1st or 2nd dose and improve over 2–4 weeks discontinuation rate 2–6% Rash 26% improves with oral antihistamines discontinuation rate 1–7% Can cause false-positive urine test results for cannabinoid with CEDIA DAU multi-level THC assay **Most significant:** Elevation in liver function tests **Teratogenicity reported in animals: not recommended in pregnant women** *(see Table 8 of the SANFORD GUIDE TO HIV/AIDS THERAPY)*
Nevirapine (Viramune)	**Most common: Rash 37%:** occurs during 1st 6 wks of therapy Women experience 7-fold ↑ in risk of severe rash *(CID 32:124, 2001)* 50% resolve within 2 wks of dc drug and 80% by 1 month 6–7% discontinuation rate **Most significant: Black Box warning—Severe life-threatening skin reactions reported:** Stevens-Johnson syndrome, toxic epidermal necrolysis and hypersensitivity reaction or drug rash with eosinophilia and systemic symptoms (DRESS) *(Arch Int Med 161:2501, 2001)* For severe rashes, dc drug immediately and do not restart In a clinical trial, the use of prednisone ↑ the risk of rash **Black Box warning—Life-threatening hepatotoxicity reported** 2/3 during the first 12 wks of rx Overall 1% develop hepatitis Pts with pre-existing ↑ in ALT or AST and/or history of chronic Hep B or C ↑ susceptible *(Hepatol 35:182, 2002)* **Women with CD4 >250, including pregnant women, at ↑ risk.** Monitor pts monthly (clinical and LFTs), esp during the first 12 wks of rx If clinical hepatotoxicity severe skin or hypersensitivity reactions occur, dc drug and never rechallenge A cohort study of nevirapine tolerance in French Aquitaine has been reported *(CID 35:1231, 2002)*.

[1] **Black Box warning for all nucleoside/nucleotide RTIs: lactic acidosis/hepatic steatosis, potentially fatal**

TABLE 14D (2)

DRUG NAME(S): GENERIC (TRADE)	ADVERSE EFFECTS
Protease Inhibitors (PI)	Abnormalities in glucose metabolism, dyslipidemias, fat redistribution syndromes are potential problems. Pts taking PI may be at increased risk for developing osteopenia/osteoporosis. *(See Table 6C of the SANFORD GUIDE TO HIV/AIDS THERAPY)* Spontaneous bleeding episodes have been reported in HIV+ pts with hemophilia being treated with PI. Rheumatoid complications have been reported with use of PIs *(An Rheum Dis 61 82, 2002)*. **Warnings for PIs:** Co-administration with drugs highly dependent on CYP3A for elimination, where ↑ levels can cause serious/life-threatening toxicity, is contraindicated.
Amprenavir (Agenerase)	**Most common:** Nausea 43–74%, vomiting 24–34%, diarrhea 39–60%, paresthesias 26–31% **Most significant:** Skin rash 22%. Most maculopapular of mild-moderate intensity, some with pruritus. Severe or life-threatening rash, including Stevens-Johnson syndrome, in 1% of pts. Skin rash onset 7–73 days, median 11 days. **Black Box warning:** ↑ potential [illegible] col toxicity with oral solution.
Atazanavir (Reyataz)	**Most common:** Asymptomatic unconjugated hyperbilirubinemia in up to 60% of pts, grade 3 & 4 in 5–9% of pts, jaundice in 17%. Diarrhea 20–25%, nausea & abdominal pain 20%, headache 25%, rash 20% **Most significant:** Prolongation of PR interval (1st degree AV block) reported.
Fosamprenavir (Lexiva)	**Most common:** Skin rash 19%, nausea 7%, diarrhea 5%, headache 2% **Most significant:** Rar[illegible] Stevens-Johnson [illegible]roma, hem[illegible]lc anemia.
Indinavir (Crixivan)	**Most common:** ↑ in indirect bilirubin 10–15% (≥2.5 mg/dl) due to a drug-induced Gilbert's syndrome (of no clinical significance). Severe hepatitis reported in 3 cases *(Ln 349 924, 1997)*. Nausea 12%, vomiting 4%, diarrhea 5%. Paronychia of big toe reported *(CID 32 140, 2001)* **Most significant: Kidney stones.** Due to indinavir crystals in collecting system (2–3% on 2 4 gm/d but higher in hot climates *(AIDS 14 296, 1997)*. 12/174 (6.9%) developed nephrolithiasis within 4 months of starting indinavir, 5/8 who continued rx had a 2nd episode *(ICAAC Abst 183, 1997)*. Prevent (minimize) by good hydration (at least 48 oz. water/day) *(AAC 42 332, 1998)*. Tubulointerstitial nephritis/renal cortical atrophy reported in association with asymptomatic ↑ urine WBC.
Nelfinavir (Viracept)	**Most common:** Mild to moderate **diarrhea** 20%. Oat bran tabs, calcium, or oral anti-diarrheal agents (e.g., loperamide, diphenoxylate/atropine sulfate) can be used to manage diarrhea.
Ritonavir (Norvir)	**Most common:** GI: bitter aftertaste ↓ by taking with chocolate milk, Ensure, or Advera; nausea 23% ↓ by initial dose escalation (titration) regimen, vomiting 13%, diarrhea 13%, circumoral paresthesias 5–6%. ↑ dose >100 mg bid assoc. with ↑ GI side-effects & ↑ in lipid abnormalities **Most significant:** Hepatic failure *(AnIM 129 670, 1998)*. **Black Box warning** relates to many important drug-drug interactions—inhibits P450 CYP3A system—may be life-threatening *(see Table 22)*.
Saquinavir (Invirase, hard cap) (Fortovase, softgel cap)	**Most common:** GI: **diarrhea** 16–20%, abdominal discomfort 9–13%, nausea 11–18%. Headache 5–9% **Black Box warning:** [illegible]nvirase is not [illegible]ivalent to Fortovase; use it [illegible] with ritonavir.
Tipranavir[NDS] (Texega)	**Most common:** Nausea & vomiting, diarrhea, abdominal pain.
Lopinavir/Ritonavir (Kaletra)	**Most common:** GI: **diarrhea** 14–24%, nausea 2–16%, lipid abnormalities in up to 30% **Most significant:** Pancreatitis, inflammato[illegible] edema of the l[illegible]s *(AIDS 16 673, 2002)*.
Fusion Inhibitor	
Enfuvirtide (T20, Fuzeon)	**Most common:** local injection site reactions (98% at least 1 local ISR, 3% dc because of ISR) (pain & discomfort, induration, erythema, nodules & cysts, pruritus & ecchymosis). Diarrhea 27%, nausea 20%, fatigue 16%. **Most significant:** ↑ rate of bacterial pneumonia (4.68 pneumonia events/100 pt yrs), hypersensitivity reactions ≤1% (rash, fever, nausea & vomiting, chills, rigors, hypotension, & ↑ serum liver transaminases).

TABLE 15A: ANTIMICROBIAL PROPHYLAXIS FOR SELECTED BACTERIAL INFECTIONS

CLASS OF ETIOLOGIC AGENT/DISEASE/CONDITION	PROPHYLAXIS AGENT/DOSE/ROUTE/DURATION	COMMENTS
Group B streptococcal disease (GBS), neonatal. Approaches to management [CDC Guidelines, *MMWR 51(RR-11):1, 2002*]:		
Pregnant women—intrapartum antimicrobial prophylaxis procedures: 1 Screen all pregnant women with vaginal & rectal swab for GBS at 35–37 wks gestation (unless other indications for prophylaxis exist GBS bacteriuria during this pregnancy or previously delivered infant with invasive GBS disease even then cultures may be useful for susceptibility testing) Use transport medium GBS survive at room temp up to 96 hrs **Rx during labor if swab culture positive.** 2 Rx during labor if previously delivered infant with invasive GBS infection, or if any GBS bacteriuria during this pregnancy *(MMWR 53 506, 2004)* 3 Rx if GBS status unknown but if any of the following are present (a) delivery at <37 wks gestation [see *MMWR 51(RR-11) 1, 2002* algorithm for threatened preterm delivery], or (b) duration of ruptured membranes ≥18 hrs or (c) intrapartum temp ≥100 4°F (≥38 0°C)		**Prophylactic regimens during labor:** **Pen G** 5 MU IV (load) then 2 5 MU IV q4h Alternate rx **Ampicillin** 2 gm IV (load) then give 1 gm IV q4h **Pen-allergic: Pts not at high risk for anaphylaxis: Cefazolin** 2 gm IV initial dose then 1 gm IV q8h **Pts at high risk for anaphylaxis:** GBS susceptible to clinda & erythro **Clindamycin** 900 mg IV q8h or **erythromycin** 500 mg IV q6h Vancomycin for pts at high risk for anaphylaxis when alternative to clindamycin or erythromycin needed (e g GBS resistant or unknown susceptibility) Continue treatment until delivery
Neonate of mother given prophylaxis	Careful observation of signs & symptoms 95% of infants will show clinical signs of infection during the 1st 24 hrs whether mother received intrapartum antibiotics or not *(Pediatrics 106 244 2000)* For gestational age <35 wks or intrapartum antibiotics <4 hrs lab evaluation (CBC diff blood culture) & ≥48 hr observation recommended See algorithm *MMWR 51(RR-11) 1, 2002*	
Preterm, premature ruptura of the membranes in Group B strep-negative women	(IV **ampicillin** 2 gm q6h + IV **erythromycin** 250 mg q6h) for 48 hrs followed by po **amoxicillin** 250 mg q8h + po **erythromycin** base 333 mg q8h x5 d Decreases infant morbidity *(JAMA 278 989 1997)*	Antibiotic rx reduced infant respiratory distress syndrome (50 6% to 40 8% p = 0 03) necrotizing enterocolitis (5 8% to 2 3% p = 0 03) and prolonged pregnancy (2 9 to 6 1 days p < 0 001) vs placebo In 1 large study (4809 pts) po erythromycin rx improved neonatal outcomes vs placebo (11 2% vs 14 4% poor outcomes p=0 02 for single births) but not co-AM/CL or both drugs in combination (both assoc with ↑ necrotizing enterocolitis) *(Ln 357 979 2001)*
Post-splenectomy bacteremia Likely agents Pneumococci (90%) meningococci H influenzae type b (also at ↑ risk of fatal malaria severe babesiosis) Ref *2003 Red Book 26th Ed Amer Acad Pediatrics*	**Immunizations:** Ensure admin of protein conjugate pneumococcal vaccine H influenzae B & quadrivalent meningococcal vaccines at recommended times In addition asplenic children with sickle cell anemia thalassemia & perhaps others daily antimicrobial prophylaxis until at least age 5—*see Comments*	Antimicrobial prophylaxis until age 5 Amox 20 mg/kg 1x/d or Pen V K 125 mg bid Over age 5 Consider Pen V-K 250 mg bid for at least 1 yr in children post splenectomy Maintain immunizations plus self-administer AM/CL with any febrile illness while seeking physician assistance Pen allergy TMP/SMX or clarithro May need to consider other alternatives if pen-resistant S pneumo prevalence increases
Sexual Exposure		
Sexual assault survivor [likely agents and risks *see NEJM 332 234 1995 MMWR 51(RR-6) 1 2002]*	[(**Ceftriaxone** 125 mg IM) + (**metronidazole** 2 gm po single dose) + [(**azithromycin** 1 gm po single dose) or (**doxycycline** 100 mg po bid x7 d)] *[MMWR 51(RR-6) 1 2002]*	Obtain expert advice re forensic exam & specimens pregnancy physical trauma psychological issues At initial exam Culture for gonococci & chlamydia (if available) wet mount for T vaginalis (& culture vaginal swab) Serologic evaluation for syphilis Hep B HIV others as appropriate Initiate HIV post-exposure protocols &/or Hep B vaccine as appropriate *(see Table 15D)* Follow-up exam for STD at 1–2 wks Retest syphilis & HIV serology at 6 12 24 wks if negative earlier
Sexual contacts likely agents N gonorrhoeae C trachomatis	[(**Ceftriaxone** 125 mg IM) + (**doxycycline** 100 mg bid po x7 d)] or [(**cefixime**[Not US] 400 mg po) + (**azithromycin** 1 gm po) each as single dose]	Be sure to check for syphilis since all regimens may not eradicate incubating syphilis Identify & rx contacts as appropriate to suspected STD *[see MMWR 51(RR-6) 1, 2002 for other etiologies & rx options]*
Syphilis exposure		Presumptive rx for exposure within 3 mos , as tests may be negative *See Table 1 page 15* Make effort to dx syphilis
Sickle-cell disease Likely agent S pneumoniae *(see post-splenectomy, above)* Ref *2003 Red Book 26th Ed , Amer Acad Pediatrics*	Children <5 yrs **Penicillin V** 125 mg po bid ≥5 yrs **Penicillin V** 250 mg po bid (Alternative in children Amoxicillin 20 mg/kg/d)	Start prophylaxis by 2 mos *(Pediatrics 106 367, 2000 http //aapredbook aappublications org)* Age appropriate vaccines including pneumococcal Hib influenza ± meningococcal Treating infections consider possibility of penicillin non-susceptible pneumococci

TABLE 15B: SURGICAL ANTIBIOTIC PROPHYLAXIS *(EID 7 220 2001 CID 38 1706 2004)*

Surgical Procedures: To be optimally effective **antibiotics must be started in the interval: 2 hrs before time of surgical incision** *(NEJM 326 281 1992)* For most procedures the number of doses needed for optimal coverage is not defined Most applications employ a single dose *(Med Lett 43 92, 2001)* although FDA approved product labeling is often for 2 or more doses If the surgical procedure lasts >3 hrs additional intraoperative doses of rapidly eliminated drugs should be given at approx 3-hr intervals A recent consensus statement from the National Surgical Infection Prevention Project *(CID 38 1706 2004)* advises antibiotic prophylaxis be started within 1 hr before incision (except vancomycin & quinolones) be supplemented intraoperatively if the procedure lasts more than 2 half-lives of the prophylactic agent and in most cases not be extended beyond 24 hrs (Note The dose/route/durations listed below for adults not intolerant of these agents are for the most part those approved in FDA product labeling For single dose regimens, the dose, time & route are the same)

TYPE OF SURGERY	PROPHYLAXIS	COMMENTS
Cardiovascular Surgery Antibiotic prophylaxis in cardiovascular surgery has been proven beneficial only in the following procedures • Reconstruction of abdominal aorta • Procedures on the leg that involve a groin incision • Any vascular procedure that inserts prosthesis/foreign body • Lower extremity amputation for ischemia • Cardiac surgery • Perhaps permanent pacemakers *(see Comment)*	**Cefazolin** 1 gm IV as a single dose or q8h x1–2 d or **cefuroxime** 1 5 gm IV as a single dose or q12h for total of 6 gm or **vancomycin** 1 gm IV as single dose Consider **intranasal mupirocin** evening before day of surgery & bid x5 days post-op in pts with pos nasal culture for S aureus	Single injection just before surgery probably as effective as multiple doses Not recommended for cardiac catheterization For prosthetic heart valves, customary to stop prophylaxis either after removal of retrosternal drainage catheters or just a 2nd dose after coming off bypass Vancomycin may be preferable in hospitals with ↑ frequency of MRSA or in high-risk pts *(CID 38 1555, 2004)* or those colonized with MRSA *(CID 38 1706 2004)* however does not cover Gm-neg bacilli therefore would add cefazolin for groin incisions Meta-analysis failed to demonstrate overall superiority of vancomycin over β-lactam prophylaxis for cardiac surgery *(CID 38 1357 2004)* A meta-analysis of 7 placebo-controlled randomized studies of antimicrobial prophylaxis for implantation of permanent pacemakers sig ↓ in incidence of infection *(Circ 97 1796 1998)* Intranasal mupirocin ↓ sternal wound infections from S aureus in 1850 pts used historical controls *(Ann Thoracic Surg 71 1572, 2001)* In another trial it reduced nosocomial S aureus infections only in nasal carriers *(NEJM 346 1871, 2002)*
Gastric, Biliary and Colonic Surgery **Gastroduodenal/Biliary** Gastroduodenal includes percutaneous endoscopic gastrostomy (high-risk only *see Comments)*	**Cefazolin** or **cefoxitin** or **cefotetan** or **ceftizoxime** or **cefuroxime** 1 5 gm IV as a single dose (some give additional doses q12h x2–3 d)	Gastroduodenal High risk is marked obesity obstruction ↓ gastric acid or ↓ GI motility
Biliary includes laparoscopic cholecystectomy (high-risk only *see Comments)*	In biliary surgery, cefazolin 1 gm & ceftizoxime 1 gm (± repeat dosing at 12 & 24 hrs) were equivalent *(AAC 40 70, 1996)*	Biliary Cephalosporins not active vs enterococci yet clinically effective as prophylaxis in biliary surgery With cholangitis treat as infection not prophylaxis TC/CL 3 1 gm q4–6h IV or (PIP/TZ 3 375 gm q6h or 4 5 gm q8h IV) or AM/SB 3 0 gm q6h IV Biliary high-risk age >70 acute cholecystitis non functioning gallbladder obstructive jaundice or common duct stones Meta-analysis supports use in percutaneous endoscopic gastrostomy *(Am J Gastro 95 3133 2000)*
Endoscopic retrograde cholangiopancreatography Controversial No benefit from single dose piperacillin in randomized placebo-controlled trial *AnIM 125 442 1996 (see Comment)*	No rx without obstruction If obstruction **Ciprofloxacin** 500–750 mg po 2 hrs prior to procedure or **Ceftizoxime** 1 5 gm IV 1 hr prior to procedure or **Piperacillin** 4 gm IV 1 hr prior to procedure	Most studies show that **achieving adequate drainage** will prevent postprocedural cholangitis or sepsis and no further benefit from prophylactic antibiotics With inadequate drainage antibiotics may be of value American Society for GI Endoscopy recommends use for known or suspected biliary obstruction Oral CIP as effective as cephalosporins in 2 studies & less expensive *(CID 23 380, 1996)*
Colorectal, Includes appendectomy Elective surgery Emergency surgery	**Neomycin** + **erythromycin** po *(see Comment for dose)* [**Cefazolin** 1–2 gm IV + **metronidazole** 0 5 gm IV (single dose)] or **cefoxitin** or **cefotetan** 1–2 gm IV	Elective colorectal prep Pre-op day (1) 10 am 4 L polyethylene glycol electrolyte solution (Colyte GoLYTELY) po over 2 hr (2) Clear liquid diet only (3) 1 pm 2 pm and 11 pm neomycin 1 gm + erythro base 1 gm po (4) NPO after midnight There are alternative regimens which have been less well studied GoLYTELY 1–6 pm then neomycin 2 gm po + metronidazole 2 gm po at 7 pm and 11 pm Oral regimen as effective as parenteral parenteral in addition to oral not required For emergency colorectal surgery use parenteral *(CID 15 Suppl 1 S313, 1992)*
Ruptured viscus *See Peritoneum/Peritonitis Secondary Table 1 Page 31*		
Head and Neck Surgery *(Ann Otol Rhinol Laryngol 101 Suppl 16 1992)* Antimicrobial prophylaxis in head & neck surgery appears efficacious only for procedures involving oral/pharyngeal mucosa (i e laryngeal or pharyngeal tumor) but even with prophylaxis wound infection rate high (41% in 1 center) *(Head Neck 23 447 2001)* Uncontaminated head & neck surgery does not require prophylaxis	**Cefazolin** 2 gm IV (single dose) or [**clindamycin** 600–900 mg IV (single dose) + **gentamicin** 1 5 mg/kg IV (single dose)]	

TABLE 15B (2)

TYPE OF SURGERY	PROPHYLAXIS	COMMENTS
Neurosurgical Procedures [Prophylaxis not effective in ↓ infection rate with intracranial pressure monitors in retrospective analysis of 215 pts *(J Neurol Neurosurg Psych 69 381 2000)*]		
Clean, non-implant, e.g., craniotomy	**Cefazolin** 1 gm IV x1. Alternative **vanco** 1 gm IV x1	Reference *Ln 344 1547, 1994*
Clean, contaminated (cross sinuses or naso/oropharynx)	**Clindamycin** 900 mg IV (single dose)	British recommend amoxicillin/clavulanate 1.2 gm IV[NUS] or (cefuroxime 1.5 gm IV + metronidazole 0.5 gm IV)
CSF shunt surgery, controversial (Meta-analysis *CID 17 98, 1993*)	**Vancomycin** 10 mg into cerebral ventricles + **gentamicin** 3 mg into cerebral ventricles *(Ln 344 1547, 1994)*	Efficacy when infection rate >15%. Alternative: TMP (160 mg) + SMX (800 mg) IV pre-op and q12h x3 doses
Obstetric/Gynecologic Surgery		
Vaginal or abdominal hysterectomy	**Cefazolin** 1–2 gm or **cefoxitin** 1–2 gm or **cefotetan** 1–2 gm or **cefuroxime** 1.5 gm all IV 30 min. before surgery	1 study found cefotetan superior to cefazolin *(CID 20 677, 1995)* For prolonged procedures, doses can be repeated q4–8h for duration of procedure
Cesarean section for premature rupture of membranes or active labor	**Cefazolin** x1, administer IV as soon as umbilical cord clamped	Not effective in elective C-section in a large prospective double-blind randomized trial *(BJOG 108 143 2001)*. However, meta-analysis of 7 trials suggested benefit *(Am J Ob Gyn 184 656, 2001)*
Abortion	1st trimester, high-risk only *(see Comments)*: aqueous **pen G** 2 mU IV or **doxycycline** 300 mg po 2nd trimester: **Cefazolin** 1 gm IV	High-risk: Pts with previous pelvic inflammatory disease, gonorrhea or multiple sexual partners *(Drugs 41 19, 1991)*
Orthopedic Surgery (Generally pts with prosthetic joints do not require prophylaxis for dental procedures. Individual considerations prevail *(J Am Dental Assn 128 1004, 1997)*. *See Table 1, page 22*		
Hip arthroplasty,[1] spinal fusion	Same as cardiac	Customarily stopped after Hemovac removed
Total joint replacement (other than hip)	**Cefazolin** 1–2 gm IV pre-op (± 2nd dose) or **vancomycin** 1 gm IV on call to OR	Post-op: some would give no further rx *(Med Lett 39 98, 1997)*
Open reduction of closed fracture with internal fixation	**Ceftriaxone** 2 gm IV or IM x1 dose	3.6% vs 8.3% (for placebo) infection found in Dutch trauma trial *(Lancet 347 1133, 1996)*
Peritoneal Dialysis Catheter Placement	**Vancomycin** single 1000 mg dose 12 hrs prior to procedure	Effectively reduced peritonitis during 14 days post-placement in 221 pts: vanco 1%, cefazolin 7%, placebo 12% (p=0.02) *(Am J Kidney Dis 36 1014, 2000)*
Urologic Surgery/Procedures		
Antimicrobials not recommended in pts with sterile urine. Pts with pre-operative bacteriuria should be treated	Recommended antibiotic to pts with pre-operative bacteriuria: **Cefazolin** 1 gm IV q8h x1–3 doses perioperatively, followed by oral antibiotics (**nitrofurantoin** or **TMP/SMX**) until catheter is removed or for 10 d. Modify based on susceptibility test results	
Transrectal prostate biopsy	**Ciprofloxacin** 500 mg po 12 hrs prior to biopsy and repeated 12 hrs after 1st dose (levo, norflox should work)	CIP reduced bacteremia from 37% (in gentamicin-rx group) to 7% *(Urology 38 84, 1991 and review in JAC 39 115, 1997)*
Other		
Breast surgery, herniorrhaphy	**P Cefo 1,2**, dosage as *Gynecologic Surgery*, above	

[1] Gentamicin (1.2.5 mg/gm of acrylic bone cement) is released for at least 3 weeks. Usefulness not proven

TABLE 15C: ANTIMICROBIAL PROPHYLAXIS FOR THE PREVENTION OF BACTERIAL ENDOCARDITIS IN PATIENTS WITH UNDERLYING CARDIAC CONDITIONS

[These are the recommendations of the American Heart Association (JAMA 277:1794, 1997). However, a population-based prospective case-controlled study brings into serious question whether dental procedures predispose to endocarditis and whether antibiotic prophylaxis is of any value (see AnIM 129:761, 1998, Br Dent J 189:610, 2000)]

ENDOCARDITIS PROPHYLAXIS RECOMMENDED	ENDOCARDITIS PROPHYLAXIS NOT RECOMMENDED
Cardiac conditions associated with endocarditis **High-risk conditions:**[1] Prosthetic valves—bioprosthetic and homograft as well as mechanical Previous bacterial endocarditis Complex cyanotic congenital heart disease e.g. single ventricle, transposition tetralogy of Fallot Surgically constructed systemic pulmonic shunts or conduits Moderate-risk conditions Most other congenital heart abnormalities or acquired valvular disease, hypertrophic cardiac myopathy, mitral prolapse with regurgitation	Negligible-risk (same as general population) Atrial septal defect (secundum) or repaired ASD/VSD or PDA (beyond 6 months) Previous CABG, mitral prolapse without MI *(see discussion JAMA 277:1794, 1997)* Physiologic, functional, or innocent heart murmurs Previous Kawasaki or rheumatic fever without valve dysfunction Cardiac pacemakers (all) and implanted defibrillators
ENDOCARDITIS PROPHYLAXIS RECOMMENDED	**ENDOCARDITIS PROPHYLAXIS NOT RECOMMENDED**
Dental and other procaduras where prophylaxis is considered for patients with moderate- or high-risk cardiac conditions Dental: Extractions, periodontal procedures[1] Implants, root canal, subgingival antibiotic fibers/strips Initial orthodontic bands (not brackets), intraligamentary local anesthetic Cleaning of teeth/implants if bleeding anticipated Respiratory: T&A, surgery on respiratory mucosa, rigid bronchoscopy GI: Sclerotherapy of esophageal varices, dilation of esophageal stricture, ERCP with biliary obstruction Biliary tract surgery, surgery on/through intestinal mucosa GU: Prostate surgery, cystoscopy, urethral dilatation	Dental: Filling cavities with local anesthetic Placement of rubber dams, suture removal, orthodontic removal Orthodontic adjustments, dental x-rays Shedding of primary teeth Respiratory: Intubation, flexible bronchoscopy[2], tympanostomy tube GI: Transesophageal cardiac echo[2], EGD without biopsy[2] GU: Vaginal hysterectomy[2], vaginal delivery[2], C-section If uninfected: Foley catheter, uterine D&C, therapeutic abortion, tubal ligation, insert/remove IUD Other: Cardiac cath, balloon angioplasty, implanted pacemaker, defibrillators, coronary stents Skin biopsy, circumcision

Abbreviations: T&A = tonsillectomy/adenoidectomy **ERCP** = endoscopic retrograde cholangiography **ASD/VSD** = atrial septal defect/ventricular septal defect **PDA** = patent ductus arteriosus **EGD** = esophagogastroduodenoscopy **D&C** = dilation and curettage

PROPHYLACTIC REGIMENS FOR DENTAL, ORAL, RESPIRATORY TRACT, OR ESOPHAGEAL PROCEDURES

SITUATION	AGENT	REGIMEN[3]
Standard general prophylaxis	Amoxicillin	Adults: 2 gm; children: 50 mg/kg orally 1 hr before procedure
Unable to take oral medications	Ampicillin	Adults: 2 gm IM or IV; children: 50 mg/kg IM or IV within 30 min before procedure
Allergic to penicillin	Clindamycin OR	Adults: 600 mg; children: 20 mg/kg orally 1 hr before procedure
	(Cephalexin[4] or cefadroxil[4]) OR	Adults: 2 gm; children: 50 mg/kg orally 1 hr before procedure
	Azithromycin or clarithromycin	Adults: 500 mg; children: 15 mg/kg orally 1 hr before procedure
Allergic to penicillin and unable to take oral medications	Clindamycin OR	Adults: 600 mg; children: 20 mg/kg IV within 30 min before procedure
	Cefazolin[4]	Adults: 1 gm; children: 25 mg/kg IM or IV within 30 min, before procedure

[1] Some now recommend that for adults, prophylaxis prior to dental procedures should **only** be used for **extractions** and **gingival surgery** (including implant replacement) and **only** for patients with **prosthetic cardiac valves** or **previous endocarditis** *(AnIM 129:829, 1998)*. If any of these 4 conditions exist = prophylactic antibiotics according to American Heart Association are recommended

[2] Prophylaxis optional for high risk patients

[3] Total children's dose should not exceed adult dose

[4] Cephalosporins should not be used in individuals with immediate type hypersensitivity reaction (urticaria, angioedema, or anaphylaxis) to penicillins

TABLE 15C (2)

PROPHYLACTIC REGIMENS FOR GENITOURINARY/GASTROINTESTINAL (EXCLUDING ESOPHAGEAL) PROCEDURES

SITUATION	AGENT	REGIMEN[1]
High risk patients	**Ampicillin + gentamicin**	**Adults: ampicillin** 2 gm IM or IV + **gentamicin** 1 5 mg/kg (not to exceed 120 mg) within 30 min of starting the procedure 6 hr later **ampicillin** 1 gm IM/IV or **amoxicillin** 1 gm orally **Children ampicillin** 50 mg/kg IM or IV (not to exceed 2 0 gm) + **gentamicin** 1 5 mg/kg within 30 min of starting the procedure 6 hrs later **ampicillin** 25 mg/kg IM/IV or **amoxicillin** 25 mg/kg orally
High risk patients allergic to ampicillin/amoxicillin	**Vancomycin + gentamicin**	**Adults: vancomycin** 1 gm IV over 1 2 hrs + **gentamicin** 1 5 mg/kg IV/IM (not to exceed 120 mg) complete injection/infusion within 30 min of starting the procedure **Children: vancomycin** 20 mg/kg IV over 1 2 hrs + **gentamicin** 1 5 mg/kg IV/IM complete injection/ infusion within 30 min of starting the procedure
Moderate risk patients	**Amoxicillin** or **ampicillin**	**Adults: amoxicillin** 2 gm orally 1 hr before procedure or **ampicillin** 2 gm IM/IV within 30 min of starting the procedure **Children amoxicillin** 50 mg/kg orally 1 hr before procedure or **ampicillin** 50 mg/kg IM/IV within 30 min of starting the procedure
Moderate-risk patients allergic to ampicillin/ amoxicillin	**Vancomycin**	**Adults: vancomycin** 1 gm IV over 1 2 hrs complete infusion within 30 min of starting the procedure **Children: vancomycin** 20 mg/kg IV over 1 2 hrs complete infusion within 30 min of starting the procedure

[1] Total children s dose should not exceed adult dose

TABLE 15D MANAGEMENT OF EXPOSURE TO HIV-1 AND HEPATITIS

OCCUPATIONAL EXPOSURE TO BLOOD, PENILE/VAGINAL SECRETIONS WITH RISK OF TRANSMISSION OF HEPATITIS B/C AND/OR HIV-1 (E.G., NEEDLESTICK INJURY)

[Adapted from *MMWR 50(RR-11) 1 2001* and *NEJM 348 826 2003*]

Free consultation for occupational exposures, call (PEPline) 1-888-HIV-4911.

General steps in management:

1 Wash clean wounds/flush mucous membranes immediately (use of caustic agents or squeezing the wound is discouraged data lacking regarding antiseptics)

2 Assess risk by doing the following (a) Characterize exposure, (b) Determine/evaluate source of exposure by medical history risk behavior & testing for hepatitis B/C HIV (c) Evaluate and test exposed individual for hepatitis B/C & HIV

Hepatitis B Exposure *[See CDC recommendations MMWR 50(RR 11), 2001]*

Exposed Person	Exposure Source		
	HBs Ag+	HBs Ag–	Status Unknown
Unvaccinated	Give HBIG 0 06 ml/kg IM & initiate HB vaccine	Initiate HB vaccine	Initiate HB vaccine and if possible check HBs Ag of source person
Vaccinated (antibody status unknown)	Do anti-HBs on exposed person If titer ≥10 MIU/ml, no rx If titer <10 MIU/ml give HBIG + 1 dose HB vaccine	No rx necessary	Do anti-HBs on exposed person If titer ≥10 MIU/ml no rx If titer <10 MIU/ml give 1 dose of HB vaccine (plus 1 dose HBIG if source high risk)

For known vaccine series responder (titer ≥10 MIU/ml) monitoring of levels or booster doses not currently recommended Known non responder (<10 MIU/ml) to 1° series HB vaccine & exposed to either HBsAg+ source or suspected high risk source—rx with HBIG & re initiate vaccine series **or** give 2 doses HBIG 1 month apart For non responders after a 2° vaccine series, 2 doses HBIG 1 month apart is preferred approach to new exposure *[MMWR 40(RR 13) 21 2001]*

Hepatitis C Exposure

Determine antibody to hepatitis C for both exposed person and if possible exposure source If source + follow-up HCV testing advised **No recommended prophylaxis** immune serum globulin not effective Monitor for early infection as therapy may ↓ risk of progression to chronic hepatitis *See Table 14 and discussion in Clin Micro Rev 16 546 2003*

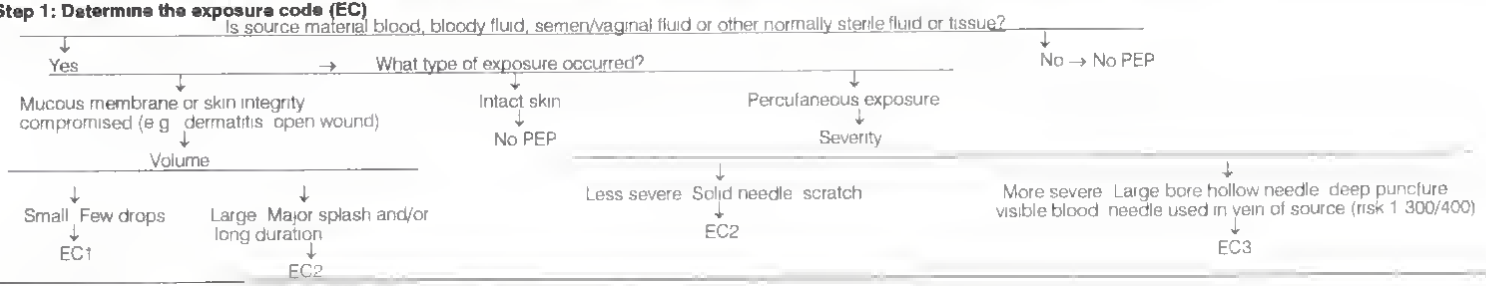
TABLE 15D (2)

HIV: Occupational exposure management *(for non-occupational HIV exposures, see www hivguidelines org/public_html/center/clinical guidelines/pep_guidelines/pep_guidelines htm)*

- The decision to initiate post-exposure prophylaxis (PEP) for HIV is a clinical judgment that should be made in concert with the exposed healthcare worker (HCW) It is based on
  1. Likelihood of the source patient having HIV infection ↑ with history of high-risk activity—injection drug use sexual activity with known HIV+ person unprotected sex with multiple partners (either hetero- or homosexual) receipt of blood products 1978–1985 ↑ with clinical signs suggestive of advanced HIV (unexplained wasting night sweats thrush seborrheic dermatitis etc) Remember the vast majority of persons are **not** infected with HIV (1/200 women infected in larger U S cities) and likelihood of infection **extremely rare** if not in above risk groups
  2. Type of exposure (approx 1 in 300–400 needlesticks from infected source will transmit HIV)
  3. Limited data regarding efficacy of PEP (PEP with ZDV alone reduced transmission by >80% in 1 retrospective case-controlled study—*NEJM 337 1485, 1997)*
  4. Significant adverse effects of PEP drugs
- If source person is **known positive for HIV** or **likely to be infected** and **status of exposure warrants PEP** antiretroviral drugs should be started **immediately** (at least within 72 hrs) If source person ELISA for HIV is negative drugs can be stopped unless source is suspected of having acute HIV infection The HCW should be re-tested at **3–4 weeks, 3 & 6 months whether PEP is used or not** (the vast majority of seroconversions will occur by 3 months delayed conversions after 6 months are exceedingly rare) Tests for HIV RNA should not be used for dx of HIV infection because of false-positives (esp at low titers) & these tests are only approved for established HIV infection [a possible exception is if pt develops signs of acute HIV (mononucleosis like) syndrome within the 1st 4–6 wks of exposure when antibody tests might still be negative]
- PEP for HIV is usually given for **4 weeks** and monitoring of adverse effects recommended baseline **complete blood count, renal and hepatic panel** to be **repeated at 2 weeks** 50–75% of HCW on PEP demonstrate mild side-effects (nausea diarrhea myalgias headache etc) but in up to ⅓ severe enough to discontinue PEP *(Antivir Ther 3 195, 2000)* Consultation with infectious diseases/HIV specialist valuable when questions regarding PEP arise Seek expert help in special situations such as pregnancy renal impairment

3 Steps to HIV Post-Exposure Prophylaxis (PEP) After Occupational Exposure: *(MMWR 50 RR-11, 2001)*

Step 1: Determine the exposure code (EC)



Step 2: Determine the HIV Status Code (HIV SC)

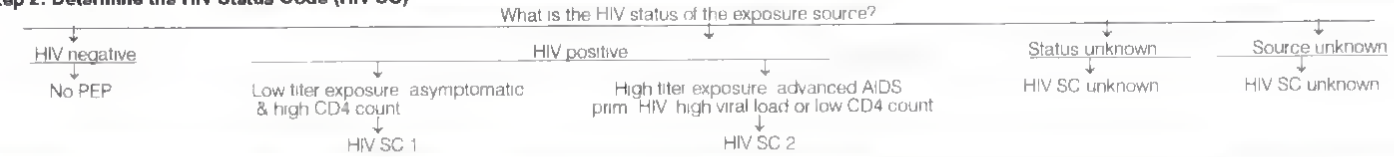


TABLE 15D (3)

Step 3. Determine Post-Exposure Prophylaxis (PEP) Recommendation

EC	HIV SC	PEP
1	1	Consider basic regimen[1]
1	2	Recommend basic regimen[1]
2	1	Recommend basic regimen[1]
2	2	Recommend expanded regimen[1]
3	1 or 2	Recommend expanded regimen[1]
1 2 3	Unknown	If exposure setting suggests risks of HIV exposure consider basic regimen[1]

Around the clock, urgent expert consultation available from:
National Clinicians' Post-Exposure Prophylaxis Hotline
(PEPline) at 1-888-448-4911 (1-888-HIV-4911)

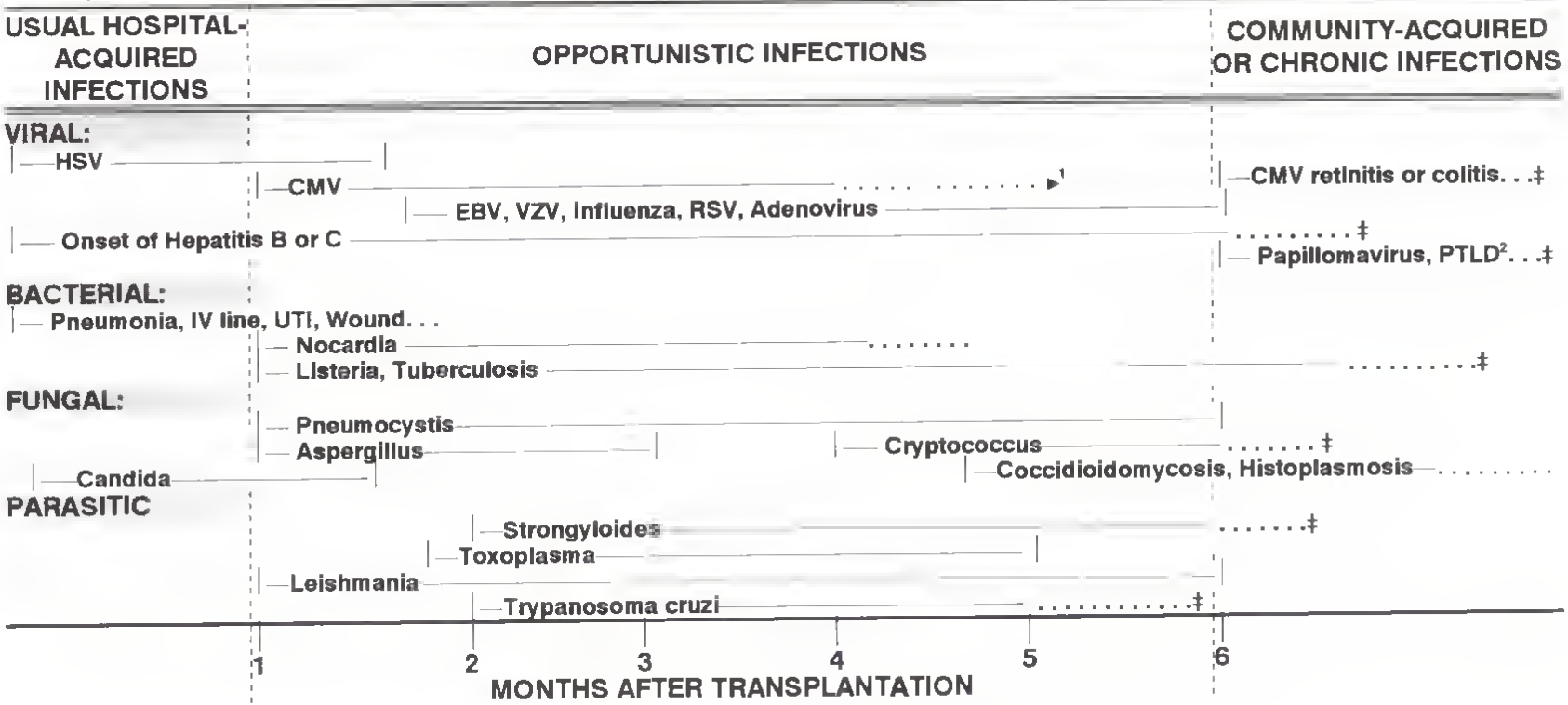
[1] **Regimens:** (Treat for 4 weeks monitor for drug side effects q2 weeks)
Basic regimen. ZDV + 3TC. or d4T + 3TC. Best to avoid ddI + d4T (↑ side effects)
Expanded regimen: Basic regimen + one of the following:. nelfinavir, lopinavir/ritonavir, indinavir (or indinavir/ritonavir): abacavir or afavirenz could be used but generally avoided in this setting. [Do not use navirapine: 22 HCWs receiving drug had serious adverse effects including 3 with hapatic necrosis *(MMWR 49 1153 2001)*.]
Other regimens can be designed. If possible, use 2 antiretroviral drugs that source pt (if known) is not currently taking or for which resistance is unlikely based on auceptibility data or treatment history. Seek expert consultation.
NOTE: Some authorities feel that an expanded regimen should be employed whenever PEP is indicated *(NEJM 349 1091 2003 & NY State AIDS Institute 2004)* For example the latter recommends ZDV + 3TC + tenofovir (*http://www.hivguidelines.org/public.html/center/clinical guidelines/pep.guidelines/pep.guidelines.htm*)

TABLE 15E PREVENTION OF OPPORTUNISTIC INFECTION IN HUMAN STEM CELL TRANSPLANTATION (HSCT) OR SOLID ORGAN TRANSPLANTATION (SOT)

General comments See Table 15F page 130 for typical timing of infections post transplant References *MMWR 49(RR-10) 1 2000 CID 33 S26 2001 COID 17 353 2004*

OPPORTUNISTIC INFECTION (at risk)	TYPE OF TRANSPLANT	PROPHYLACTIC REGIMENS	COMMENTS/REFERENCES
Herpes simplex (seropositive)	HSCT	Acyclovir 200 mg po 3x/d from conditioning to engraftment or resolution of mucositis	Do not need acyclovir if receiving CMV prophylaxis
	SOT	Acyclovir 200 mg po 3x/d —start early post-transplant	
CMV (Recipient + OR Donor + Recipient –)	HSCT	Universal (Recipient +) Ganciclovir 5 mg/kg IV q12h x5–7d then 5–6 mg/kg 1 x/d 5 days/wk x100 days Preemptive (Donor + recipient neg) 1–2 x/wk screen plasma for either (1) CMV antigen or (2) CMV DNA by PCR—when positive, start ganciclovir as for Universal, above For general review see *Clin Micro Rev 16 647 2003*	
	SOT	Kidney kidney/pancreas heart Valganciclovir 900 mg po 1x/d by day 10 to day 100 post transplant Liver Ganciclovir 1000 mg po tid by day 10 to day 100 post-transplant Lung (Ganciclovir 5 mg/kg IV q12h x5–7 d + CMV-immune globulin 150 mg/kg within 72 hrs then at 2 4 6 & 8 wks post-transplant then 100 mg/kg at wks 12 & 16) then valganciclovir 900 mg po 1x/d x6 months	
Hepatitis B-induced cirrhosis	Liver	Lamivudine 100 mg po 1x/d 4 wks pre-transplant & 12 months post-transplant	Some have combined with HBIG *(Hepatol 28 585 1998)*
Candida sp.	Liver	Fluconazole 200–400 mg IV/po 1x/d starting before transplant & continuing up to 3 mos in high-risk pts Optimal duration unknown Concerns for ↑ non albicans candida with fluconazole prophylaxis *(Transpl 75 2023 2003)*	
	HSCT	Fluconazole 400 mg po 1x/d from day 0 to engraftment or ANC >1000	
Aspergillus sp.	Lung/Heart-lung	No controlled trials to determine optimal management Randomized trial suggested ABLC better tolerated than Ampho B deoxycholate if nebulized route is used[NUS] *(Transpl 77 232 2004)*	
Coccidioides immitis	All	Reasonable Fluconazole 400 mg po 1x/d *(Transpl Inf Dis 5 3 2003)*	
Pneumocystis carinii (P. jiroveci) & Toxoplasma gondii	All	TMP/SMX SS or –DS 1 tab po 1x/d Duration 4 mos –1 yr renal ≥6 mos for allogenic HSCT ≥1 yr to lifetime for heart, lung liver Breakthrough infections reported with atovaquone doses <1500 mg/d *(CID 38 e76, 2004)*	
Trypanosoma cruzi	Heart	If known Chagas disease in donor or recipient, contact CDC for nifurtimox	

TABLE 15F
TEMPORAL APPROACH TO DIFFERENTIAL DIAGNOSIS OF INFECTION AFTER ORGAN TRANSPLANTATION*



* Adapted from Fishman and Rubin *NEJM 338 1741, 1998* For hematopoietic stem cell transplant recipients *see MMWR 49 RR 10 2000*
‡ Solid lines indicate usual time period for onset of infection dotted lines indicate risk at reduced level

[1] Symptomatic CMV antigenemia may be delayed in patients receiving 3 mo ganciclovir prophylaxis *(Transpl Inf Dis 6 3 2004)*
[2] **PTLD** = Post transplant lymphoproliferative disease.

TABLE 16: PEDIATRIC DOSAGES OF SELECTED ANTIBACTERIAL AGENTS

[Adapted from (1) Nelson's Pocket Book of Pediatric Antimicrobial Therapy, 2002-2003, 15th Ed., J. Bradley & J. Nelson, eds , Lippincott Williams and Wilkins, and (2) 2003 Red Book, 26th Ed., American Academy of Pediatrics, pages 700–718

DRUG	DOSES IN MG/KG/D OR MG/KG AT FREQUENCY INDICATED[1]				
	BODY WEIGHT <2000 gm		BODY WEIGHT >2000 gm		>28 DAYS OLD
	0–7 days old	8–28 days old	0–7 days old	8–28 days old	
Aminoglycosides IV or IM (check levels some dose by gestational age + wks of life see *Nelson's Pocket Book page 19*)					
Amikacin	7.5 q18–24h	7.5 q12h	10 q12h	10 q12h	10 q8h
Gent/tobra	2.5 q18–24h	2.5 q12h	2.5 q12h	2.5 q12h	2.5 q8h
Aztreonam IV	30 q12h	30 q8h	30 q8h	30 q6h	30 q6h
Cephalosporins					
Cefaclor					20–40 div tid
Cefadroxil					30 div bid (max 2 g/d)
Cefazolin	20 q12h	20 q12h	20 q12h	20 q8h	20 q8h
Cefdinir					7 q12h or 14 qd
Cefepime					150 div q8h
Cefixime					8 as qd or div bid
Cefotaxime	50 q12h	50 q8h	50 q12h	50 q8h	50 q6h (75 q6h for meningitis)
Cefoxitin			20 q12h		80–160 div q6h
Cefpodoxime					10 div bid (max 400 mg/d)
Cefprozil					15–30 div bid (max 1 g/d)
Ceftazidime	50 q12h	50 q8h	50 q12h	50 q8h	50 q8h
Ceftibuten					4.5 bid
Ceftizoxime					33–66 q8h
Ceftriaxone	50 qd	50 qd	50 qd	75 qd	50–75 qd (meningitis 100)
Cefuroxime IV	50 q12h	50 q8h	50 q8h	50 q8h	50 q8h (80 q8h for meningitis)
po					10–15 bid (max 1 g/d)
Cephalexin					25–50 div 4x/d (max 4 g/d)
Loracarbef					15–30 div bid (max 0.8 g/d)
Chloramphen IV	25 q24h	25 q24h	25 q24h	15 q12h	12.5–25 q6h (max 2–4 g/d)
Clindamycin IV	5 q12h	5 q8h	5 q8h	5 q6h	7.5 q6h
po					5–6 q8h
Ciprofloxacin po[2]					20–30 div bid (max 1.5 g/d)
Imipenem[3] IV			25 q12h	25 q8h	15–25 q6h (max 2 g/d)
Linezolid	No data	10 q8h	No data	10 q8h	10 q8h to age 12
Macrolides					
Erythro IV & po	10 q12h	10 q8h	10 q12h	13 q8h	10 q6h
Azithro po					10–12 day 1 then 5/d[4]
Clarithro po					7.5 q12h (max 1 g/d)
Meropenem IV	20 q12h	20 q8h	20 q12h	20 q8h	60–120 div q8h (120 for meningitis)
Metro IV & po	7.5 q24h	7.5 q12h	7.5 q12h	15 q12h	7.5 q6h
Penicillins					
Ampicillin	50 q12h	50 q8h	50 q8h	50 q6h	50 q6h
Amp sulbactam					100–300 div q6h
Amoxicillin po				30 div bid	25–50 div tid
Amox Clav po	30 div bid	30 div bid	30 div bid	30 div bid	45 or 90 (AM/CL-HD) div bid if over 12 wks of age
Cloxacillin					50–100 div 4x/d
Dicloxacillin					12–25 div 4x/d
Mezlocillin	75 q12h	75 q8h	75 q12h	75 q8h	75 q6h
Nafcillin,oxacillin IV	25 q12h	25 q8h	25 q8h	37 q6h	37 q6h (to max 8–12 gm/d)
Piperacillin PIP/tazo IV	75 mg/kg q12h	75 mg/kg q12h	75 mg/kg q8h	75 mg/kg q8h	100–300 div q4–6h
Ticarcillin T clav IV	75 q12h	75 q8h	75 q8h	75 q6h	75 q6h
Penicillin G **U/kg** IV	50,000 q12h	75,000 q8h	50,000 q8h	50,000 q6h	50,000 U/kg/d
Penicillin V					25–50 mg/kg/d div 3–4x/d
Rifampin po			10, single dose	20, single dose	20 single dose (max 600 mg)
Sulfisoxazole po				120–150	120–150 mg/kg/d div q4–6h
TMP/SMX po IV UTI 8–12 TMP component div bid, Pneumocystis 20 TMP component div 4x/d					
Tetracycline po (age 8 or older)					25–50 div 4x/d
Doxycycline po IV (age 8 or older)					2–4 div bid
Vancomycin IV	12.5 q12h	15 q12h	18 q12h	22 q12h	40–60 div q6h

Abbreviations **Chloramphen** = chloramphenicol **Clav** = clavulanate **div** = divided **Gent/tobra** = gentamicin/tobramycin **Metro** = metronidazole **Tazo** = tazobactam **TMP** = trimethoprim **TMP/SMX** = trimethoprim/sulfamethoxazole **UTI** = urinary tract infection

[1] May need higher doses in patients with meningitis *see CID 39 1267, 2004*
[2] With exception of cystic fibrosis not approved for use under age 18
[3] Not recommended in children with CNS infections due to risk of seizures
[4] Dose for otitis for pharyngitis 12 mg/kg x5 d

TABLE 17A: DOSAGE OF ANTIMICROBIAL DRUGS IN ADULT PATIENTS WITH RENAL IMPAIRMENT

Adapted from DRUG PRESCRIBING IN RENAL FAILURE 4th Ed Aronoff et al (Eds) American College of Physicians 1999 and Berns et al Renal Aspects of Antimicrobial Therapy for HIV Infection In P Kenmel & J Berns Eds HIV INFECTION AND THE KIDNEY Churchill-Livingstone 1995 pp 195–236

UNLESS STATED, ADJUSTED DOSES ARE % OF DOSE FOR NORMAL RENAL FUNCTION.

Drug adjustments are based on the patient's estimated endogenous creatinine clearance which can be calculated as

$$\frac{(140-\text{age})(\text{ideal body weight in kg})}{(72)(\text{serum creatinine mg/dL})} \text{ for men (x 0 85 for women)}$$

Ideal body weight for men 50 0 kg + 2 3 kg per inch over 5 feet

Ideal body weight for women 45 5 kg + 2 3 kg per inch over 5 feet

For alternative method to calculate estimated CrCl *see AnIM 130 461 1999*

NOTE: For summary of drugs requiring ***no*** dosage adjustment with renal insufficiency *see Table 17B page 137*

ANTIMICROBIAL	HALF-LIFE (NORMAL/ESRD) hr	DOSE FOR NORMAL RENAL FUNCTION[5]	METHOD* *(see footnote)*	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min >50–90	10–50	<10	SUPPLEMENT FOR HEMODIALYSIS, CAPD *(see footnote)*	COMMENTS AND DOSAGE FOR CAVH†
ANTIBACTERIAL ANTIBIOTICS								
Aminoglycoside Antibiotics‖		**Traditional multiple daily doses—adjustment for renal disease**						
Amikacin	1 4–2 3/17–150	7 5 mg/kg q12h	D&I	60–90% q12h	30–70% q12 18h **Same dose for CAVH†**	20–30% q24–48h	HEMO Extra ½ of normal renal function dose AD+ CAPD 15–20 mg lost/L dialysate/day¶ *(see Comment)*	High flux hemodialysis membranes lead to unpredictable aminoglycoside clearance measure post-dialysis drug levels for efficacy and toxicity With CAPD pharmacokinetics highly variable— **check serum levels** ¶Usual method for CAPD 2 liters of dialysis fluid placed qid or 8 liters/day (give 8Lx20 mg lost/L = 160 mg of amikacin supplement IV per day)
Gentamicin Tobramycin	2–3/20–60	1 7 mg/kg q8h	D&I	60–90% q8–12h	30–70% q12h **Same dose for CAVH†**	20–30% q24–48h	HEMO Extra ½ of normal renal function dose AD+ CAPD 3–4 mg lost/L dialysate/day	
Netilmicin[NUS]	2–3/35–72	2 0 mg/kg q8h	D&I	50–90% q8–12h	20–60% q12h **Same dose for CAVH†**	10–20% q24–48h	HEMO Extra ½ of normal renal function dose AD+ CAPD 3–4 mg lost/L dialysate/day	Adjust dosing weight for obesity [Ideal body weight + 0 4(actual body weight – ideal body weight)] *(CID 25 112 1997)*
Streptomycin	2–3/30–80	15 mg/kg (max of 1 0 gm) q24h	I	50% q24h	q24–72h **Same dose for CAVH†**	q72–96h	HEMO Extra ½ of normal renal function dose AD+ CAPD 20–40 mg lost/L dialysate/day	**Example: CrCl 0 on hemodialysis:** 60 kg pt Initial dose of 1 7 mg/kg = 102 mg Then 12–18 mg q48h with extra 51 mg AD+

ONCE-DAILY AMINOGLYCOSIDE THERAPY: ADJUSTMENT IN RENAL INSUFFICIENCY *(see Table 10C for OD dosing/normal renal function)*

Creatinine Clearance (ml/min)	>80	60–80	40–60	30–40	20–30	10–20	<10–0
Drug	Dose q24h (mg/kg)					Dose q48h (mg/kg)	Dose q72h and AD+
Gentamicin/Tobramycin	5 1	4	3 5	2 5	4	3	2
Amikacin/kanamycin/streptomycin	15	12	7 5	4	7 5	4	3
Isepamicin[N]	8	8	8	8 q48h	8	8 q72h	8 q96h
Netilmicin	6 5	5	4	2	3	2 5	2 0

Carbapenem Antibiotics							
Ertapenem	4/~4	1 0 gm q24h	D	1 0 gm q24h	0 5 gm q24h (CrCl <30)	0 5 gm q24h	HEMO Dose as for CrCl <10 if dosed <6 hrs prior to HD give 150 mg supplement AD+
Imipenem *(see Comment)*	1/4	0 5 gm q6h	D&I	250–500 mg q6–8h	250 mg q6–12h **Same dose for CAVH†**	125–250 mg q12h	HEMO Dose AD+ CAPD Dose for CrCl ~ 10 ↑ potential for seizures if recommended doses exceeded in pts with CrCl <20 ml/ min See pkg insert esp for pts <70 kg
Meropenem	1/6–8	1 0 gm q8h	D&I	1 0 gm q8h	1 0 gm q12h **Same dose for CAVH†**	0 5 gm q24h	HEMO Dose AD+ CAPD Dose for CrCl ~ 10

† **CAVH** continuous arteriovenous hemofiltration *(NEJM 336 1303 1997)* usually results in CrCl of approx 30 ml/min * **AD** after dialysis **"Dose AD" refers to timing of dose**

See page 136 for other footnotes and abbreviations **Supplement is to replace drug lost via dialysis; extra drug beyond continuation of regimen used for CrCl <10 ml/min.**

TABLE 17A (2)

ANTIMICROBIAL	HALF-LIFE (NORMAL/ESRD) hr	DOSE FOR NORMAL RENAL FUNCTION[1]	METHOD* (see footnote)	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min >50–90	10–50	<10	SUPPLEMENT FOR HEMODIALYSIS, CAPD† (see footnote)	COMMENTS AND DOSAGE FOR CAVH†
Cephalosporin Antibiotics: DATA ON SELECTED **PARENTERAL** CEPHALOSPORINS								
Cefazolin	1.9/40–70	1.0–2.0 gm q8h	I	q8h	q12h **Same dose for CAVH†**	q24–48h	HEMO Extra 0.5–1 gm AD+ CAPD 0.5 gm q12h	
Cefepime	2.2/18	2.0 gm q8h (max. dose)	D&I	2 gm q8h	2 gm q12–24h **Same dose for CAVH†**	1 gm q24h	HEMO Extra 1 gm AD+ CAPD 1–2 gm q48h	CAVH† dose As for CrCl 10–50
Cefotaxime Ceftizoxime	1.7/15–35	2.0 gm q8h	I	q8–12h	q12–24h **Same dose for CAVH†**	q24h	HEMO Extra 1 gm AD+ CAPD 0.5–1 gm qd	Active metabolite of cefotaxime in ESRD ↓ dose further for hepatic & renal failure
Cefotetan	3.5/13–25	1–2 gm q12h	D	100%	50%	25%	HEMO Extra 1 gm AD+ CAPD 1 gm qd	CAVH† dose 750 mg q12h
Cefoxitin	0.8/13–23	2.0 gm q8h	I	q8h	q8–12h **Same dose for CAVH†**	q24–48h	HEMO Extra 1 gm AD+ CAPD 1 gm qd	May falsely increase serum creatinine by interference with assay
Ceftazidime	1.2/13–25	2 gm q8h	I	q8–12h	q24–48h **Same dose for CAVH†**	q48h	HEMO Extra 1 gm AD+ CAPD 0.5 gm qd	Volume of distribution increases with infection
Cefuroxime sodium	1.2/17	0.75–1.5 gm q8h	I	q8h	q8–12h	q24h	HEMO Dose AD+ CAPD Dose for CrCl <10	CAVH† dose 1.5 gm then 750 mg IV q24h
Fluoroquinolone Antibiotics								
Ciprofloxacin	4/6–9	500–750 mg po (or 400 mg IV) q12h	D	100%	50–75%	50%	HEMO 250 mg po or 200 mg IV q12h CAPD 250 mg po or 200 mg IV q8h	CAVH† dose 200 mg IV q12h
Gatifloxacin	7–14/36	400 mg po/IV q24h	D	400 mg q24h	200 mg q24h **Same dose for CAVH†**	200 mg q24h	HEMO 200 mg q24h AD+ CAPD 200 mg q24h	CAVH† dose As for CrCl 10–50
Gemifloxacin	7/>7	320 mg po qd	D	320 mg qd	160 mg qd	160 mg qd	HEMO 160 mg qd AD+ CAPD 160 mg qd	
Levofloxacin	4–8/76	500 mg qd IV PO	D†	100%	500 mg x1 then 250 q24–48h	500 mg x1 then 250 q48h	HEMO/CAPD Dose for CrCl <10	CAVH† dose As for CrCl 10–50
Ofloxacin	7.0/28–37	400 mg po/IV q12h	D&I	100%	200–400 mg q12h	200 mg q24h	HEMO 100–200 mg AD+ CAPD Dose for CrCl <10	CAVH† dose 300 mg/d
Macrolide Antibiotics								
Clarithromycin	5–7/22	0.5–1.0 gm q12h	D	100%	75%	50–75%	HEMO Dose AD+ CAPD None	ESRD dosing recommendations based on extrapolation
Erythromycin	1.4/5–6	250–500 mg q6h	D	100%	100%	50–75%	HEMO/CAPD/CAVH† None	Ototoxicity with high doses in ESRD Vol. of distribution increases in ESRD
Miscelleneous Antibecterial Anbbiotics								
Colistin	?	80–160 mg q8h	D	160 mg q12h	160 mg q24h	160 mg q36h	HEMO 80 mg AD+	
Daptomycin	9.4/30	4 mg/kg/d	I	4 mg/kg/d	CrCl <30 4 mg/kg q48h		HEMO & CAPD 4 mg/kg q48h (after dialysis if possible)	
Linezolid	6.4/7.1	600 mg po/IV q12h	None	600 mg q12h	600 mg q12h	600 mg q12h AD+	HEMO As for CrCl <10 CAPD No data	CAVH† No data Accumulation of 2 metabolites—risk unknown
Metronidazole	6–14/7–21	7.5 mg/kg q6h	D	100%	100% **Same dose for CAVH†**	50%	HEMO Dose AD+ CAPD Dose for CrCl <10	Hemo clears metronidazole and its metabolites *(AAC 29 235, 1986)*
Nitrofurantoin	0.5/1	50–100 mg	D	100%	Avoid	Avoid	Not applicable	
Sulfamethoxazole	10/20–50	1.0 gm q8h	I	q12h	q18h Same dose for CAVH†	q24h	HEMO Extra 1 gm AD+ CAPD 1 gm qd	

† Regardless of CrCl 1st dose is 500 mg and then adjust dose and interval

‡ **CAVH** = continuous arteriovenous hemofiltration *(NEJM 336:1303, 1997)* usually results in CrCl of approx. 30 ml/min + **AD** = after dialysis **"Dose AD" refers to timing of dose.**

See page 136 for other footnotes and abbreviations **Supplement is to replace drug lost via dialysis; extra drug beyond continuation of regimen used for CrCl <10 ml/min.**

TABLE 17A (3)

ANTIMICROBIAL	HALF-LIFE (NORMAL/ESRD) hr	DOSE FOR NORMAL RENAL FUNCTION[a]	METHOD* (see footnote)	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min >50–90	10–50	<10	SUPPLEMENT FOR HEMODIALYSIS, CAPD+ (see footnote)	COMMENTS AND DOSAGE FOR CAVH[f]
Miscellaneous Antibacterial Antibiotics *(continued)*								
Teicoplanin[NUS]	45/62–230	6 mg/kg/day	I	q24h	q48h **Same dose for CAVH[f]**	q72h	HEMO Dose for CrCl <10 CAPD Dose for CrCl <10	
Telithromycin	10/15	800 mg qd	D	800 mg qd	400 mg qd (<30 ml/min)	400 mg qd	HEMO 800 mg AD+ CAPD No data	
Trimethoprim	11/20–49	100–200 mg q12h	I	q12h	q18h **Same dose for CAVH[f]**	q24h	HEMO Dose AD+ CAPD q24h	CAVH[f] dose q18h
Vancomycin[1]	6/200–250	1 gm q12h	D&I	1 gm q12h	1 gm q24–96h	1 gm q4–7 d	HEMO/CAPD Dose for CrCl <10	CAVH[f] 500 mg q24–48h New hemodialysis membranes ↑ clear of vanco check levels
Penicillins								
Amoxicillin Ampicillin	1.0/5–20 1.0/7–20	250–500 mg q8h 250 mg–2 gm q6h	I I	q8h q6h	q8–12h q6–12h	q24h q12–24h	HEMO Dose AD+ CAPD 250 mg q12h	IV amoxicillin not available in the U.S.
Amoxicillin/ Clavulanate[2]	1.3 AM/1.0 5–20/4.0	500/125 mg q8h *(see Comments)*	D&I	500/125 mg q8h	250–500 mg AM component q12h	250–500 mg AM component q24h	HEMO As for CrCl <10 extra dose after dialysis	**if CrCl ≤30/ml, do not use 875/125 or 1000/62.5 AM/CL products**
Ampicillin (AM)/ Sulbactam(SB)	1.0 (AM)/1.0 (SB) 9.0 (AM)/10.0 (SB)	2 gm AM + 1.0 gm SB q6h	I	q6h	q8–12h	q24h	HEMO Dose AD+ CAPD 2 gm AM/1 gm SB q24h	CAVH[f] dose 1.5 AM/0.75 SB q12h
Aztreonam	2.0/6–8	2 gm q8h	D	100%	50–75% **Same dose for CAVH[f]**	25%	HEMO Extra 0.5 gm AD+ CAPD Dose for CrCl <10	Technically is a β-lactam antibiotic
Penicillin G	0.5/6–20	0.5–4 million U q4h	D	100%	75% **Same dose for CAVH[f]**	20–50%	HEMO Dose AD+ CAPD Dose for CrCl <10	1.7 mEq potassium/mU ↑ potential for seizures 6 mU/d upper limit dose in ESRD
Piperacillin	1.0/3.3–5.1	3–4 gm q4–6h	I	q4–6h	q6–8h **Same dose for CAVH[f]**	q8h	HEMO Dose AD+ CAPD Dose for CrCl <10	1.9 mEq sodium/gm
Pip (P)/Tazo(T)	1.0 P/1.0 T 3.0 P/4.0 T	3.375 gm q6h	D&I	3.375 gm q6h	2.25 gm q6h	2.25 gm q8h	HEMO Dose for CrCl <10 + 0.75 gm AD+ CAPD Dose for CrCl <10	
Ticarcillin	1.2/13	3 gm q4h	D&I	1–2 gm q4h	1.2 gm q8h **Same dose for CAVH[f]**	1.2 gm q12h	HEMO Extra 3.0 gm AD+ CAPD Dose for CrCl <10	5.2 mEq sodium/gm
Ticarcillin/ Clavulanate[2]	1.0 (TC)/1.0(CL) 13 (TC)/4.0 (CL)	3.1 gm q4h	D&I	3.1 gm q4h	2.0 gm q4–8h	2.0 gm q12h	HEMO Extra 3.1 gm AD+ CAPD 3.1 gm q12h	*See footnote 2*
Tetracycline Antibiotics								
Tetracycline	6–10/57–108	250–500 mg qid	I	q8–12h	q12–24h	q24h	HEMO/CAPD/CAVH[f] None	Avoid in ESRD
ANTIFUNGAL ANTIBIOTICS								
Amphotericin B & ampho B lipid complex	24/unchanged	Non lipid 0.4–1.0 mg/kg/d ABCC[3] 3–6 mg/kg/d ABLC[3] 5 mg/kg/d LAB[3] 3–5 mg/kg/d	I	q24h	q24h **Same dose for CAVH[f]**	q24–48h	HEMO None CAPD Dose for CrCl <10	For ampho B toxicity lessened by saline loading; risk amplified by concomitant cyclosporine A, aminoglycosides, or pentamidine
Fluconazole	37/100	200–400 mg q24h	D	200–400 mg q24h	100–200 mg q24h **Same dose for CAVH[f]**	100–200 mg q24h	HEMO 100% of recommended dose AD+ CAPD Dose for CrCl <10	
Flucytosine	3–6/75–200	37.5 mg/kg q6h	I	q12h	q12–24h **Same dose for CAVH[f]**	q24h	HEMO Dose AD+ CAPD 0.5–1.0 gm q24h	Goal is peak serum level >25 μg/ml and <100 μg/ml

[1] Vancomycin serum levels may be overestimated in renal failure if measured by either fluorescence polarization immunoassay or radioimmunoassay; vanco breakdown products interfere. EMIT method OK.
[2] Clavulanate cleared by liver, not kidney. Hence as dose of combination decreased, a deficiency of clavulanate may occur *(JAMA 285:386, 2001)*.
[3] **ABCC** = ampho B cholesteryl complex; **ABLC** = ampho B lipid complex; **LAB** = liposomal ampho B.
[f] **CAVH** = continuous arteriovenous hemofiltration *(NEJM 336:1303, 1997)* usually results in CrCl of approx. 30 ml/min. + **AD** = after dialysis. **"Dose AD" refers to timing of dose.**

See page 136 for other footnotes and abbreviations. **Supplement is to replace drug lost via dialysis; extra drug beyond continuation of regimen used for CrCl <10 ml/min.**

TABLE 17A (4)

ANTIMICROBIAL	HALF-LIFE (NORMAL/ESRD) hr	DOSE FOR NORMAL RENAL FUNCTION[1]	METHOD* (see footnote)	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min			SUPPLEMENT FOR HEMODIALYSIS, CAPD (see footnote)	COMMENTS AND DOSAGE FOR CAVH[‡]
				>50–90	10–50	<10		
ANTIFUNGAL ANTIBIOTICS *(continued)*								
Itraconazole po soln	35/	100–200 mg q12h		100%	100%	100%	HEMO/CAPD/CAVH[‡] No adjustment with oral solution	
Itraconazole IV	35/	200 mg IV q12h		200 mg IV bid	Do not use IV itra if CrCl <30 due to accumulation of carrier cyclodextrin			
Terbinafine	36 200/?	250 mg po/day	–	q24h	Use has not been studied Recommend avoidance of drug			
Voriconazole IV	Non linear kinetics	6 mg/kg IV q12h x2 then 4 mg/kg q12h		No change	If CrCl <50 ml/min accum of IV vehicle (cyclodextrin) Switch to po or DC			
ANTIPARASITIC ANTIBIOTICS								
Pentamidine	29/118	4 mg/kg/d	I	q24h	q24h	q24–36h	HEMO/CAPD/CAVH[‡] None	
Quinine	5–16/5–16	650 mg q8h	I	650 mg q8h	650 mg q8 12h **Same dose for CAVH[‡]**	650 mg q24h	HEMO Dose AD[+] CAPD Dose for CrCl <10	Marked tissue accumulation
ANTITUBERCULOUS ANTIBIOTICS *(Excellent review Nephron 64 169 1993)*								
Ethambutol	4/7 15	15–25 mg/kg q24h	I	q24h **Same dose for CAVH[‡]**	q24–36h	q48h	HEMO Dose AD[+] CAPD Dose for CrCl <10	25 mg/kg 4–6 hr prior to dialysis for usual 3x/wk dialysis Streptomycin recommended in lieu of ethambutol in renal failure
Ethionamide	2 1/?	250–500 mg q12h	D	100%	100%	50%	HEMO/CAPD/CAVH[‡] None	
Isoniazid	0 7 4/8–17	5 mg/kg/d (max 300 mg)	D	100%	100%	100%	HEMO Dose AD[+] CAPD/CAVH[‡] Dose for CrCl <10	
Pyrazinamide	9/26	25 mg/kg q24h (max dose 2 5 gm qd)	D	25 mg/kg q24h	25 mg/kg q24h	12–25 mg/kg q24h	HEMO 25–35 mg/kg after each dialysis CAPD No reduction CAVH[‡] No data	
Rifampin	1 5–5/1 8–11	600 mg/d	D	600 mg q24h	300–600 mg q24h	300–600 mg q24h	HEMO None CAPD/CAVH[‡] Dose for CrCl <10	Biologically active metabolite
ANTIVIRAL AGENTS								
Acyclovir IV	2 5/20	5–12 4 mg/kg q8h	D&I	5–12 4 mg/kg q8h	5–12 4 mg/kg q12 24h	2 5 mg/kg q24h	HEMO Dose AD[+] CAPD Dose for CrCl <10	Rapid IV infusion can cause renal failure CAVH[‡] dose 3 5 mg/kg/d
Adefovir		10 mg po qd	I	10 mg qd	10 mg q48–72h	10 mg q7 days	HEMO q7d AD[+]	
Amantadine	12/500	100 mg po bid	I	q24–48h	q48–72h	q7d	HEMO/CAPD/CAVH[‡] None	
Cidofovir Complicated dosing—*see package insert*								
Induction	2 5/unknown	5 mg/kg 1x/wk for 2 wks	–	5 mg/kg 1x/wk	0 5–2 mg/kg 1x/wk	0 5 mg/kg 1x/wk	No data	Major toxicity is renal No efficacy safety or pharmacokinetic data in pts with moderate/severe renal disease
Maintenance	2 5/unknown	5 mg/kg q2wks	–	5 mg/kg q2wks	0 5–2 mg/kg q2wks	0 5 mg/kg q2wks	No data	
Didanosine tablets[1]	0 6–1 6/4 5	125–200 mg q12h buffered tabs	D	200 mg q12h	200 mg q24h	<60 kg 150 mg q24h >60 kg 100 mg q24h	HEMO Dose AD[+] CAPD/CAVH[‡] Dose for CrCl <10	Based on incomplete data Data are estimates
		400 mg qd enteric-coated tabs	D	400 mg qd	125–200 mg qd	**Do not use EC tabs**	HEMO/CAPD Dose for CrCl <10	**If <60 kg & CrCl <10 ml/min, do not use EC tabs**
Emtricitabine	10/>10	200 mg qd	I	200 mg qd	200 mg q48–72h	200 mg q96h	HEMO Dose for CrCl <10	

[1] Ref for NRTIs and NNRTIs *Kidney International 60 821, 2001*

[‡] **CAVH** = continuous arteriovenous hemofiltration *(NEJM 336 1303 1997)* usually results in CrCl of approx 30 ml/min * **AD** = after dialysis **"Dose AD" refers to timing of dose.**

See page 136 for other footnotes and abbreviations **Supplement is to replace drug lost via dialysis; extra drug beyond continuation of regimen used for CrCl <10 ml/min.**

TABLE 17A (5)

ANTIMICROBIAL	HALF-LIFE (NORMAL/ESRD) hr	DOSE FOR NORMAL RENAL FUNCTION§	METHOD* (see footnote)	ADJUSTMENT FOR RENAL FAILURE Estimated creatinine clearance (CrCl), ml/min			SUPPLEMENT FOR HEMODIALYSIS, CAPD+ (see footnote)	COMMENTS AND DOSAGE FOR CAVH‡
				>50–90	10–50	<10		
ANTIVIRAL AGENTS *(continued)*								
Famciclovir	2 3–3 0/10–22	500 mg q8h	D&I	500 mg q8h	500 mg q12–24h **Same dose for CAVH‡**	250 mg q24h	HEMO Dose AD+ CAPD No data	CAVH‡ dose As for CrCl 10–50
				CrCl as ml/min/kg body weight—ONLY FOR FOSCARNET				
				>1.4	>1.0–1.4	>0.8–1.0 >0.6–0.8 >0.5–0.6	>0.4–0.5	<0.4
Foscarnet (CMV dosage) *Dosage adjustment based on est CrCl (ml/min) div by pt s kg*	Normal half life (T½) 3 hrs with terminal T½ of 18–88 hrs T ½ very long with ESRD	Induction 60 mg/kg q8h x2–3 wks IV Maintenance 90–120 mg/kg/d IV		60 q8h 120 q24h	45 q8h 90 q24h	50 q12h 65 q24h 40 q12h 105 q48h 60 q24h 80 q48h	50 q24h 65 q48h	Do not use Do not use
Ganciclovir	2 9/30	Induction 5 mg/kg q12h IV	D&I	5 mg/kg q12h	1 25–2 5 mg/kg q24h	1 25 mg/kg 3x/wk	HEMO Dose AD+ CAPD Dose for CrCl <10	
	IV	Maintenance 5 mg/kg q24h IV	D&I	2 5–5 0 mg/kg q24h	0 6–1 25 mg/kg q24h	0 625 mg/kg 3x/week	HEMO 0 6 mg/kg AD+ CAPD Dose for CrCl <10	
	po	1 0 gm tid po	D&I	0 5–1 gm tid	0 5–1 0 gm qd	0 5 gm 3x/week	HEMO 0 5 gm AD+	
Indinavir/nelfinavir/nevirapine		No data on influence of renal insufficiency Less than 20% excreted unchanged in urine Probably no dose reduction						
Lamivudine¶	5–7/15–35	300 mg po qd	D&I	300 mg po qd	50–150 mg qd	25 50 mg qd	HEMO Dose AD+ CAPD/CAVH‡ No data	
Oseltamivir	1–3/no data	75 mg po bid	I	75 mg q12h	75 mg qd	No data	No data	
Ribavirin	Use with caution in patients with creatinine clearance <10 ml/min							
Rimantadine	13 65/Prolonged	100 mg bid po	I	100 mg bid	100 mg qd–bid	100 mg qd recommended	HEMO/CAPD No data	Use with caution little data
Ritonavir & Saquinavir SGC				Negligible renal clearance At present no patient data				
Stavudine po¶	1 1 4/5 5–8	30–40 mg q12h	D&I	100%	50% q12–24h **Same dose for CAVH‡**	≥60 kg 20 mg/d <60 kg 15 mg/d	HEMO Dose as for CrCl <10 AD+ CAPD No data	CAVH‡ dose As for CrCl 10–50
Tenofovir		300 mg q24h		300 mg q24h	**DO NOT USE IF CrCl <60 ml/min.**			
Valacyclovir	2 5–3 3/14	1 0 gm q8h	D&I	1 0 gm q8h	1 0 gm q12–24h **Same dose for CAVH‡**	0 5 gm q24h	HEMO Dose AD+ CAPD Dose for CrCl <10	CAVH‡ dose As for CrCl 10–50
Valganciclovir	4/67	900 mg po bid	D&I	900 mg po bid	450 mg qd to 450 mg qod	DO NOT USE		
Zalcitabine¶	2 0/>8	0 75 mg q8h	D&I	0 75 mg q8h	0 75 mg q12h **Same dose for CAVH‡**	0 75 mg q24h	HEMO Dose AD+ CAPD No data	CAVH‡ dose As for CrCl 10–50
Zidovudine¶	1 1 1 4/1 4–3	300 mg q12h	D&I	300 mg q12h	300 mg q12h	100 mg q6–8h if hemo AD+	HEMO Dose for CrCl <10 CAPD Dose for CrCl <10	CAVH‡ dose 100 mg q8h

‡ **CAVH** continuous arteriovenous hemofiltration *(NEJM 336 1303 1997)* + **AD** after dialysis
Supplement is to replace drug lost via dialysis; extra drug beyond continuation of regimen used for CrCl <10 ml/min "Dose AD" refers to timing of dose
§ Dosages are for life threatening infections * **D** = dosage reduction **I** interval extension ** Per cent refers to % change from dose for normal renal function
Abbreviations: HEMO hemodialysis **CAPD** chronic ambulatory peritoneal dialysis **ESRD** = endstage renal disease **NUS** not available in the U S

¶ Ref for NRTIs and NNRTIs *Kidney International 60 821 2001*

TABLE 17B: ND DDSAGE ADJUSTMENT WITH RENAL INSUFFICIENCY, BY CATEGDRY:

Antibacterials		Antifungals	Anti-TBc	Antivirals	
				Non-HIV	Anti-HIV Druga
Azithromycin	Linezolid	Amphotericin B	Rifabutin	None	Abacavir
Ceftriaxone	Minocycline	Caspofungin	Rifapentine		Amprenavir
Chloramphenicol	Moxifloxacin	Itraconazole oral solution			fosamprenavir
Ciprofloxacin XL	Nafcillin	Voriconazole **po only**			Delavirdine
Clindamycin	Pyrimethamine				Efavirenz
Dirithromycin	Rifaximin				Lopinavir
Doxycycline					Nevirapine

TABLE 18: ANTIMICRDBIALS AND HEPATIC DISEASE DDSAGE ADJUSTMENT

The following alphabetical list indicates antibacterials excreted/metabolized by the liver **wharain a dosaga adjuatment mey be indicated** in the presence of hepatic disease. Space precludes details; consult the PDR or package inserts for details. List is **not** all-inclusive.

- Amprenavir, fosamprenavir
- Atazanavir
- Caspofungin *(Table 11B)*
- Ceftriaxone
- Chloramphenicol
- Clindamycin
- Delavirdine
- Efavirenz
- Indinavir
- Isoniazid
- Itraconazole solution
- Metronidazole
- Nafcillin
- Nevirapine
- Rifabutin
- Rifampin
- Rimantadine
- Tinidazole
- Voriconazole

TABLE 19: TREATMENT OF CAPD PERITDNITIS IN ADULTS[1]

(Periton Dial Intl 20 396 2000)

EMPIRIC Intraparitoneal Tharapy:[2] Cultura Raaults Panding

Drug		Reeidual Urina Dutput	
		<100 ml/day	>100 ml/day
Cefazolin +	Can mix in same bag	1 gm/bag qd	20 mg/kg BW/bag, qd
Ceftazidime		1 gm/bag qd	20 mg/kg BW/bag qd

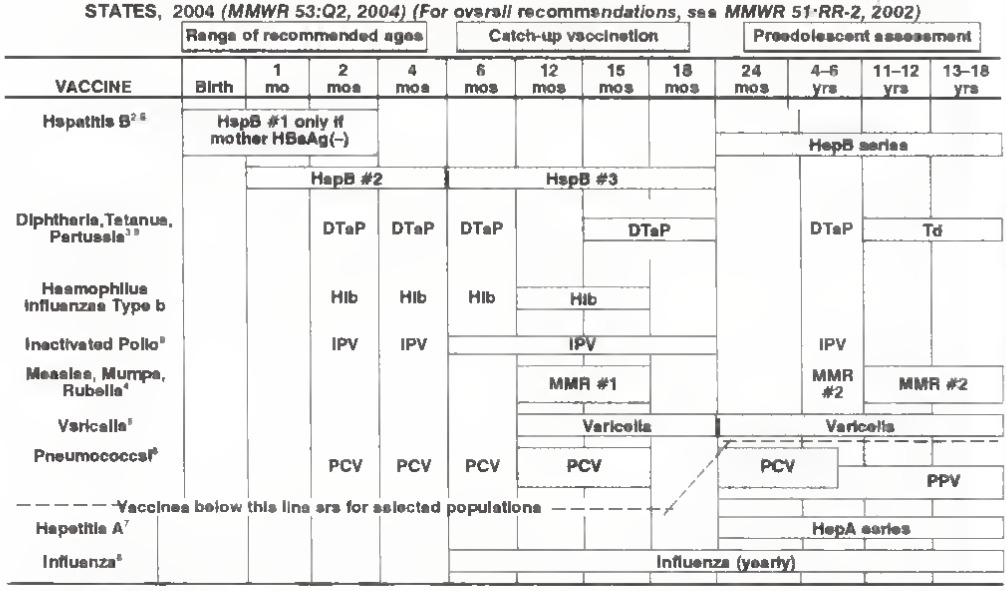
Drug Dosaa for SPECIFIC Intraparitonaal Tharapy—Cultura Raaults Known. NDTE: Faw po druga indicatad

Drug	Intermittent Dosing (onca/day)		Continuous Dosing (par litar axchanga)	
	Anuric	Non-Anuric	Anuric	Non-Anuric
Gantamicin	0.6 mg/kg	↑ dose 25%	MD 8 mg	↑ MD by 25%
Cafazolin	15 mg/kg	20 mg/kg	LD 500 mg MD 125 mg	LD 500 mg ↑ MD 25%
Ceftazidima	1000–1500 mg	ND	LD 250 mg MD 125 mg	ND
Ampicillin	250–500 mg po bid	ND	250–500 mg po bid	ND
Ciprofloxacin	500 mg po bid	ND	LD 50 mg MD 25 mg	ND
Vancomycin	15–30 mg/kg q5–7 d	↑ dose 25%	MD 30–50 mg/L	↑ MD 25%
Matronidazola	250 mg po bid	ND	250 mg po bid	ND
Amphotaricin B	NA	NA	MD 1.5 mg	NA
Fluconazole	200 mg qd	ND	200 mg qd	ND
Itraconazole	100 mg q12h	100 mg q12h	100 mg q12h	100 mg q12h
Amp/sulbactam	2 gm q12h	ND	LD 1.0 gm MD 100 mg	ND
TMP SMX	320/1600 mg po q1–2 d	ND	LD 320/1600 mg po MD 80/400 mg po qd	ND

[1] **All dosas IP unlass indicated otharwisa.**
LD = loading dose **MD** = maintenance dose **ND** = no data **NA** = not applicable—dose as normal renal function **Anuric** = <100 ml/d **non-anuric** = >100 ml/d

[2] Does not provide treatment for MRSA. If Gram-positive cocci on Gram stain, include vancomycin.

TABLE 20A: RECOMMENDED CHILDHOOD AND ADOLESCENT IMMUNIZATION SCHEDULE[1]: UNITED STATES, 2004 *(MMWR 53:Q2, 2004) (For overall recommendations, see MMWR 51/RR-2, 2002)*



[1] **Indicates age groups that warrant special effort to administer those vaccines not given previously**

[2] **Hepatitis B vaccine (HepB)** Infants born to HBsAg-positive mothers should receive hepatitis B vaccine and 0.5 ml hepatitis B immune globulin (HBIG) within 12 hours of birth at separate sites. The 2nd dose is recommended at age 1–2 months. The last dose in the vaccination series should not be administered before age 6 months. These infants should be tested for HBsAg and anti-HBs at 9–15 months of age. Infants born to mothers whose HBsAg status is unknown should receive the 1st dose of the HepB vaccine series within 12 hours of birth. Maternal blood should be drawn as soon as possible to determine the mother's HBsAg status; if the HBsAg test is positive, the infant should receive HBIG as soon as possible (no later than age 1 week). The 2nd dose is recommended at age 1–2 months. The last dose in the vaccination series should not be administered before age 6 months.

[3] **Tetanus and diphtheria toxoids (Td)** Subsequent routine Td boosters are recommended every 10 years.

[4] **Measles, mumps, and rubella vaccine (MMR)** No evidence that MMR causes autism *(NEJM 347:1477–2002)*.

[5] **Varicella vaccine** Primary vaccine failures may occur *(NEJM 347:1909–2002)*. Benefit outweighs risk *(JID 188:945–2003)*.

[6] **Pneumococcal vaccine. Pneumococcal polysaccharide vaccine (PPV)** is recommended in addition to PCV for certain high-risk groups. *See MMWR 49(RR-9):1–2000*.

[7] **Hepatitis A vaccine** Hepatitis A vaccine is recommended for children and adolescents and for certain high-risk groups *(MMWR 48(RR-12):1–1999)*.

[8] **Influenza vaccine** *[see MMWR 51(RR-3):1–2002]* Children aged ≤12 years should receive vaccine in a dosage appropriate for their age (0.25 ml if 6–35 months or 0.5 ml if ≥3 years). Children aged ≤8 years who are receiving influenza vaccine for the first time should receive 2 doses separated by at least 4 weeks. A self-limited 48 hr oculorespiratory syndrome post-vaccine recognized *(CID 37:1059 & 1136–2003)*. Trivalent (types A & B) live, cold-adapted, attenuated influenza virus vaccine (FluMist™) for intranasal application in subjects 5–49 yrs old approved by U.S. FDA 6/2003.

[9] **DTaP, HepB, IPV** available in combined vaccine (Pediarix™) which is given at 2, 4, and 6 months of age *(MMWR 52:203–2003)*.

Additional information about vaccines, including precautions and contraindications for vaccination and vaccine shortages, is available at www.cdc.gov/nip or at the National Immunization Information hotline, 800-232-2522 (English) or 800-232-0233 (Spanish). Copies of the schedule can be obtained at www.cdc.gov/nip/recs/child-schedule.htm. Approved by the **Advisory Committee on Immunization Practices** (www.cdc.gov/nip/acip), the **American Academy of Pediatrics** (www.aap.org), the **American Academy of Family Physicians** (www.aafp.org), and the **Pan American Health Organization** (www.paho.org).

Catch-Up Schedule For Children Aged 4 Months–6 Years Who Start Late Or Are >1 Month Behind

Dose 1 (minimum age)	Minimum interval between doses			
	Dose 1 to dose 2	Dose 2 to dose 3	Dose 3 to dose 4	Dose 4 to dose 5
DTaP (6 wks)	**4 wks**	**4 wks**	**6 mos.**	**6 mos.**[1]
IPV (6 wks)	**4 wks**	**4 wks**	**4 wks**[2]	
HepB[3] (birth)	**4 wks**	**8 wks** (& 16 wks after 1st dose)		
MMR (12 mos.)	**4 wks**[4]			
Varicella (12 mos.)				
Hib[5] (6 wks)	**4 wks:** if 1st dose given at age <12 mos **8 wks (as final dose):** if 1st dose given at age 12–24 mos **No further doses needed:** if 1st dose given at age ≥15 mos	**4 wks**[6]: if current age <12 mos **8 wks (as final dose)**[6]: if current age ≥12 mos & 2nd dose given at age <15 mos **No further doses needed:** if previous dose given at age ≥15 mos	**8 wks (as final dose):** this dose only necessary for children aged 12 mos–5 yrs who received 3 doses before age 12 mos	
PCV[7] (6 wks)	**4 wks:** if 1st dose given at age <12 mos & current age <24 mos **8 wks (as final dose):** if 1st dose given at age ≥12 mos or current age 24–59 mos **No further doses needed:** for healthy children if 1st dose given at age ≥24 mos	**4 wks:** if current age <12 mos **8 wks (as final dose):** if current age ≥12 mos **No further doses needed:** for healthy children if previous dose given at age ≥24 mos	**8 wks (as final dose):** this dose only necessary for children aged 12 mos–5 yrs who received 3 doses before age 12 mos	

TABLE 20A (2)

[1] **Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP).** The 5th dose is not necessary if the 4th dose was given after the 4th birthday

[2] **Inactivated polio (IPV):** For children who received an all-IPV or all-OPV series a 4th dose is not necessary if 3rd dose was given at age ≥4 yrs If both OPV and IPV were given as part of a series a total of 4 doses should be given regardless of the child's current age

[3] **Hepatitis B vaccine (HepB):** All children and adolescents who have not been vaccinated against hepatitis B should begin the hepatitis B vaccination series during any visit Providers should make special efforts to immunize children who were born in or whose parents were born in areas of the world where hepatitis B virus infection is moderately or highly endemic

[4] **Measles, mumps, and rubella vaccine (MMR):** The 2nd dose of MMR is recommended routinely at age 4–6 yrs but may be given earlier if desired

[5] **Haemophilus influenzae type b (Hib):** Vaccine is not recommended generally for children aged ≥5 years

[6] **Hib:** If current age is 12 months and the first 2 doses were PRP OMP [PedVaxHIB® or ComVax (Merck)®], the 3rd (and final) dose should be given at age 12–15 months and at least 8 weeks after the 2nd dose

[7] **Pneumococcal conjugate vaccine (PCV):** Vaccine is not recommended generally for children aged ≥5 years unless post splenectomy

Catch-Up Schedule for Children Aged 7–18 Years Who Start Late or Are >1 Month Behind

Vaccine	Minimum interval between doses		
	Dose 1 to dose 2	Dose 2 to dose 3	Dose 3 to booster dose
Td[1]	4 wks	6 mos.	**6 mos:** if 1st dose given at age <12 mos & current age <11 yrs **5 yrs:** if 1st dose given at age ≥12 mos & 3rd dose given at age <7 yrs & current age ≥11 yrs **10 yrs:** if 3rd dose given at age ≥7 yrs
IPV[2]	4 wks	4 wks	*See footnote 2 above*
HepB	4 wks	8 wks (& 16 wks after 1st dose)	
MMR	4 wks		
Varicella[3]	4 wks		

[1] **Tetanus toxoid:** For children aged 7–10 years the interval between the 3rd & booster dose is determined by the age when the 1st dose was given For adolescents aged 11–18 years the interval is determined by the age when the 3rd dose was given

[2] **Inactivated polio (IPV):** Vaccine is not recommended generally for persons aged ≥18 years

[3] **Varicella:** Give 2 dose series to all susceptible adolescents aged ≥13 years

Conjugate pneumococcal vaccine (PCV): For all infants <2 years old and high-risk children (e g , HIV asplenia nephrotic syndrome sickle cell anemia) between 2 and 5 years of age *(Med Lett 42 25 2000 PIDJ 19 181 2000 PIDJ 19 371ff 2000)* Also approved for prevention of otitis media *(Med Letter 45 27, 2003)* and for cochlear implant recipients *(MMWR 52 739 2003)* Use of vaccine associated with decline in invasive pneumococcal disease *(NEJM 348 1737 2003)*

Immunization schedule: *(see Schedule page 138)*

Age at first dose (0.5 ml)	Total number of doses	Timing
Infants	4	2 4 6 and 12–15 months
7–11 months	3	2 doses at least 4 wks apart 3rd dose after 1 year birthday separated from 2nd dose by at least 2 months
12–23 months	2	2 doses at least 2 months apart
≥24 months	1*	

* For children ≥24 months old who are chronically ill or immunosuppressed ICIP recommends 2 doses of PCV admin 2 mos apart followed by 1 dose of a 23-valent pneumococcal vaccine 2 or 3 mos after 2nd PCV dose *(MMWR 50 10 , 2001)*

TABLE 20B: ADULT IMMUNIZATION IN THE UNITED STATES *(MMWR 52 966, 2003)*

(Travelers see Med Letter 38 17 1996)

Recommended Adult Immunization Schedule—United States, 2003–2004

Vaccine	Age group (years)		
	19–49	50–64	≥65
Tetanus, diphtheria (Td)[1]	1 dose booster every 10 years		
Influenza	1 dose annually for persons with medical or occupational indications or household contacts of persons with indications	1 annual dose	
Pneumococcal (polysaccharide)	1 dose for persons with medical or other indications (1 dose revaccination for immunosuppressive conditions)[2]		1 dose for unvaccinated persons 1 dose revaccination[2]
Hepatitis B[1]	3 doses (0, 1–2, 4–6 months) for persons with medical, behavioral, occupational, or other indications[3]		
Hepatitis A	2 doses (0, 6–12 months) for persons with medical, behavioral, occupational, or other indications[4]		
Measles, mumps, rubella (MMR)[1]	1 dose if MMR vaccination history is unavailable, 2 doses for persons with occupational, geographic, or other indications[5]		
Varicella[1]	2 doses (0, 4–8 weeks) for persons who are susceptible[6]		
Meningococcal (polysaccharide)	1 dose for persons with medical or other indications[7]		

☐ For all persons in this age group ▒ For persons with medical/exposure indications ▨ Catch-up on childhood vaccinations

[1] Covered by the Vaccine Injury Compensation Program

TABLE 20B (2)

[2] Revaccination with pneumococcal polysaccharide vaccine 1-time revaccination after 5 years for persons with chronic renal failure or nephrotic syndrome functional or anatomic asplenia (e.g. sickle cell disease or splenectomy) immunosuppressive conditions (e.g. congenital immunodeficiency HIV infection leukemia lymphoma multiple myeloma Hodgkin's disease generalized malignancy & organ or bone marrow transplantation) chemotherapy with alkylating agents antimetabolites or long-term systemic corticosteroids For persons aged ≥65 yrs 1-time revaccination if they were vaccinated ≥5 yrs previously & were aged <65 yrs at the time of primary vaccination *[MMWR 46(RR-8) 1997]*

[3] Medical indications hemodialysis pts & pts who receive clotting-factor concentrates Occupational indications health-care workers & public-safety workers who are exposed to blood in the workplace persons in training in schools of medicine dentistry nursing lab technology & other allied health professions Behavioral indications injection-drug users persons with more than 1 sex partner during the preceding 6 months persons with a recently acquired STD all clients in STD clinics & men who have sex with men (MSM) Other indications household contacts & sex partners of persons with chronic hepatitis B virus (HBV) infection clients & staff of institutions for the developmentally disabled international travelers who will be located for >6 months in countries with high or intermediate prevalence of chronic HBV infection & inmates of correctional facilities *[MMWR 40(RR-13) 1991]*

[4] For the combined hepatitis A-hepatitis B vaccine use 3 doses at 0 1 & 6 months Medical indications persons with clotting factor disorders or chronic liver disease Behavioral indications MSM & users of injection-drug & noninjecting illegal drugs Occupational indications persons working with hepatitis A virus (HAV) infected primates or with HAV in a research lab setting Other indications persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A *[MMWR 48(RR-12), 1999]*

[5] Measles component Adults born before 1957 might be considered to be immune to measles Administer 2 doses of MMR for adults with at least one of the following conditions & without vaccination history • adults born after 1956 • persons vaccinated with killed-measles virus vaccine during 1963–1969 • students in post-secondary education institutions • healthcare workers • susceptible international travelers to countries in which measles is endemic Mumps component 1 dose of MMR should be adequate for protection Rubella component Administer 1 dose of MMR to women whose rubella vaccination history is unreliable & counsel women to avoid becoming pregnant for 4 weeks after vaccination For women of childbearing age regardless of birth year determine rubella immunity & counsel women routinely regarding congenital rubella syndrome Do not vaccinate pregnant women or those planning to become pregnant during the next 4 weeks If pregnant & susceptible vaccinate as early in postpartum period as possible *[MMWR 47(RR-8) 1998]*

[6] Recommended for all persons without evidence of prior varicella zoster virus (VZV) infection healthcare workers & family contacts of immunocompromised persons those who live or work in environments in which transmission is likely (e.g., teachers of young children day care employees & residents & staff members in institutional settings) persons who live or work in environments in which VZV transmission can occur (e.g. college students inmates & staff members of correctional institutions & military personnel) adolescents & adults living in households with children women who are not pregnant but who might become pregnant in the future & international travelers who are not immune to infection Do not vaccinate pregnant women or those planning to become pregnant during the next 4 weeks If pregnant & susceptible vaccinate as early in postpartum period as possible *[MMWR 45(RR-11) 1996 MMWR 48(RR-6) 1999]*

[7] Meningococcal vaccine (quadrivalent polysaccharide for serogroups A C Y & W 135) Medical indications consider vaccination for adults with terminal complement-component deficiencies or with anatomic or functional asplenia Other indications travelers to countries in which disease is hyperendemic or epidemic [e.g. the "meningitis belt" of sub-Saharan Africa & Mecca (Saudi Arabia) during Hajj] Revaccination at 3–5 years might be indicated for persons at high risk for infection (e.g. persons residing in areas in which disease is epidemic) Counsel college freshmen especially those who live in dormitories about meningococcal disease & the vaccine so that they can make an educated decision about receiving the vaccination *[MMWR 46(RR-5) 1997]* Healthcare providers need not initiate discussion of the meningococcal quadrivalent polysaccharide vaccine as part of routine medical care

Recommended Immunizations for Adults with Medical Conditions—United States, 2003–2004

Medical condition	Vaccine						
	Tetanus-diphtheria (Td)[1]	Influenza	Pneumococcal (polysaccharide)	Hepatitis B[1]	Hepatitis A	Measles, mumps, rubella (MMR)[1]	Varicella[1]
Pregnancy		A					
Diabetes, heart disease, chronic pulmonary disease, & chronic liver disease, including chronic alcoholism		B	C		D		
Congenital immunodeficiency, leukemia, lymphoma, generalized malignancy, rx with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids			E				F
Renal failure/end-stage renal disease & recipients of hemodialysis or clotting factor concentrates			E	G			
Asplenia including elective splenectomy & terminal complement-component deficiencies			E,H,I				
HIV infection			E,J			K	

For all persons in this age group | For persons with medical/exposure indications | Catch-up on childhood vaccinations | Contraindicated

[1] Covered by the Vaccine Injury Compensation Program

TABLE 20B (3)

A Vaccinate if pregnancy is at 2nd or 3rd trimester during influenza season
B Although chronic liver disease & alcoholism are not indicator conditions for influenza vaccination administer 1 dose annually if the patient is aged ≥50
C Asthma is an indicator condition for influenza but not for pneumococcal vaccination
D For all persons with chronic liver disease
E Revaccinate once if ≥5 years have elapsed since initial vaccination
F Persons with impaired humoral but not cellular immunity might be vaccinated *[MMWR 48(RR-6), 1999]*
G Hemodialysis patients Use special formulation of vaccine (40 µg/ml) or two 1 0 ml 20 µg doses administered at one site Vaccinate early in the course of renal disease Assess antibody titers to hepatitis B surface antigen (anti-HBs) levels annually Administer additional doses if anti-HBs levels decline to < 10 mIU/ml
H Also administer meningococcal vaccine consider H influenzae type b vaccine
I Elective splenectomy Vaccinate ≥2 weeks before surgery
J Vaccinate as close to diagnosis as possible when CD4 cell counts are highest
K Withhold MMR or other measles-containing vaccines from HIV-infected persons with evidence of severe immunosuppression *(MMWR 45 603 1996)*

Administration schedule for vaccines: *Review package insert for specific product being administered*

TABLE 20C/1: ANTI-TETANUS PROPHYLAXIS, WOUND CLASSIFICATION, IMMUNIZATION

WOUND CLASSIFICATION		
Clinical Features	**Tetanus Prone**	**Non-Tetanus Prone**
Age of wound	> 6 hours	≤ 6 hours
Configuration	Stellate avulsion	Linear
Depth	> 1 cm	≤ 1 cm
Mechanism of injury	Missile crush, burn frostbite	Sharp surface (glass knife)
Devitalized tissue	Present	Absent
Contaminants (dirt saliva etc)	Present	Absent

(From ACS Bull 69 22 23, 1984, No 10)

IMMUNIZATION SCHEDULE				
History of Tetanus Immunization	**Dirty, Tetanus-Prone Wound**		**Clean, Non-Tetanus Prone Wound**	
	Td[1,2]	**TIG**	**Td**	**TIG**
Unknown or < 3 doses	Yes	Yes	Yes	No
3 or more doses	No[3]	No	No[4]	No

[1] Td = Tetanus & diphtheria toxoids adsorbed (adult)
TIG = Tetanus immune globulin (human)
[2] Yes if wound >24 hours old
For children <7 years DPT (DT if pertussis vaccine contraindicated)
For persons ≥7 years Td preferred to tetanus toxoid alone
[3] Yes if >5 years since last booster
[4] Yes if >10 years since last booster

(From MMWR 39 37, 1990, MMWR 46(SS 2) 15, 1997)

TABLE 20C/2: RABIES POST-EXPOSURE PROPHYLAXIS[1] All wounds should be cleaned immediately and thoroughly with soap and water. This has been shown to protect 90% of experimental animals!
Post-Exposure Prophylaxis Guide, United States, 2000 (*CID 30:4, 2000*)

Animal Type	Evaluation and Disposition of Animal	Recommendations for Prophylaxis
Dogs cats ferrets	Healthy and available for 10-day observation	Dont start unless animal develops sx then immediately begin HRIG + HDCV or RVA
	Rabid or suspected rabid	Immediate vaccination
	Unknown (escaped)	Consult public health officials
Skunks raccoons bats * foxes coyotes most carnivores	Regard as rabid	Immediate vaccination
Livestock rodents rabbits includes hares squirrels hamsters guinea pigs gerbils, chipmunks rats, mice woodchucks		Almost never require anti-rabies rx Consult public health officials

* Most recent cases of human rabies in U S due to contact (not bites) with silver-haired bats or rarely big brown bats *(MMWR 46 770 1997 AIM 128 922 1998)* For more detail *see CID 30 4 2000 JAVMA 219 1687 2001 CID 37 96 2003 (travel medicine advisory), Lancet 363 959 2004*

Post-Exposure Rabies Immunization Schedule
IF NOT PREVIOUSLY VACCINATED

Treatment	Regimen[2]
Local wound cleaning	All post-exposure treatment should begin with immediate thorough cleaning of all wounds with soap and water
Human rabies immune globulin (HRIG)	20 IU/kg body weight given once on day 0 If anatomically feasible the full dose should be infiltrated around the wound(s) the rest should be administered IM in the gluteal area HRIG should **not** be administered in the **same syringe or** into the **same anatomical site** as vaccine or more than 7 days after the initiation of vaccine Because HRIG may partially suppress active production of antibody no more than the recommended dose should be given [3]
Vaccine	Human diploid cell vaccine (HDCV) rabies vaccine adsorbed (RVA) or purified chick embryo cell vaccine (PCEC) 1 0 ml **IM (deltoid area[4])** one each on days 0 3, 7, 14, & 28

TABLE 20C (2)

IF PREVIOUSLY VACCINATED[5]

Treatment	Regimen[2]
Local wound cleaning	All post-exposure treatment should begin with immediate thorough cleaning of all wounds with soap and water
HRIG	HRIG should **not** be administered
Vaccine	HDCV, RVA or PCEC, 1.0 ml **IM** (**deltoid area**[4]), one each on days 0 and 3

CORRECT VACCINE ADMINISTRATION SITES

Age Group	Administration Site
Children and adults	**DELTOID**[4] only (**NEVER** in gluteus)
Infants and young children	Outer aspect of thigh (anterolateral thigh) may be used (**NEVER** in gluteus)

1 From *MMWR 48 RR-1, 1999 CID 30 4 2000* B T Matyas Mass Dept of Public Health
2 These regimens are applicable for all age groups including children
3 In most reported post-exposure treatment failures only identified deficiency was failure to infiltrate wound(s) with HRIG *(CID 22 228, 1996)* However several failures reported from SE Asia in patients in whom WHO protocol followed *(CID 28 143 1999)*
4 The **deltoid** area is the **only** acceptable site of vaccination for adults and older children For infants and young children the outer aspect of the thigh (anterolateral thigh) may be used Vaccine should **NEVER** be administered in the gluteal area
5 Any person with a history of pre-exposure vaccination with HDCV RVA PCEC prior post-exposure prophylaxis with HDCV RVA, PCEC or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination

TABLE 21: SELECTED DIRECTORY OF RESOURCES

ORGANIZATION	PHONE/FAX	WEBSITE(S)
ANTIPARASITIC DRUGS and PARASITOLOGY INFORMATION *(CID 37 694 2003)*		
CDC	Weekdays 404 639 3670 Evenings weekends holidays	www cdc gov/ncidod/srp/drugs/drug service html 404-639 2888
DPDx Lab ID of parasites		www dpd cdc gov/dpdx/default htm
Gorgas Course Tropical Medicine		http //info dom uab edu/gorgas
Panorama Compound Pharm	800 247-9767/818-787 7256	www uniquerx com
Parasites and Health		www dpd cdc gov/dpdx/HTML/Para_Health htm
BIOTERRORISM		
Centers for Disease Control & Prevention	770 488-7100	www bt cdc gov
Infectious Diseases Society of America	703-299 0200/ 703 299-0204	www idsociety org
Johns Hopkins Center Civilian Biodefense		www jhsph edu
Center for Biosecurity of the Univ of Pittsburgh Med Center		www upmc-biosecurity org
US Army Medical Research Institute of Inf Dis		www usamriid army mil
HEPATITIS C *(CID 35 754 2002)*		
CDC		www cdc gov/ncidod/diseases/hepatitis/C
Individual		http //hepatitis-central com
Medscape		www medscape com
HIV		
General		
HIV inSite		http //hivinsite ucsf edu
Johns Hopkins AIDS Service		www hopkins-aids edu
Drug Interactions		
Johns Hopkins AIDS Service		www hopkins aids edu
Liverpool HIV Pharm Group		www hiv druginteractions org
Other		http //AIDS medscape com
Prophylaxis/Treatment of Opportunistic Infections HIV Treatment		www aidsinfo nih gov
IMMUNIZATIONS *(CID 36 355 2003)*		
CDC Natl Immunization Program	404-639 8200	www cdc gov/nip
FDA Vaccine Adverse Events	800 822 7967	www fda gov/cber/vaers/vaers htm
National Network Immunization Info	877-341 6644/ 703 299-0204	www immunizationinfo org
Influenza vaccine CDC	404 639 8200	www cdc gov/nip/flu
Institute for Vaccine Safety		www vaccinesafety edu
OCCUPATIONAL EXPOSURE, BLOOD-BORNE PATHOGENS (HIV, HEPATITIS B & C)		
National Clinicians Post Exposure Hotline	888-448-4911	www ucsf edu/hivcntr
Q-T_c INTERVAL PROLONGATION BY DRUGS		www qtdrugs org
SEXUALLY TRANSMITTED DISEASES		www cdc gov/std/treatment/TOC2002TG htm
	Slides	www hc-sc gc ca/pphb dgspsp/std mts
TRAVELERS' INFO: Immunizations, Malaria Prophylaxis, More		
Amer Soc Trop Med & Hyg		www astmh org
CDC general	877 394 8747/888 232-3299	www cdc gov/travel/index htm
CDC, Malaria		www cdc gov/ncidod/dpd/parasites/malaria/default htm
Prophylaxis	888 232-3228	www cdc gov/travel
Treatment	770-488 7788	www who int/health_topics/malaria
MD Travel Health		www mdtravelhealth com
Pan American Health Organization		www paho org
World Health Organization (WHO)	(41 22) 791 2122/ (00-41 22)-691-0746	www who int/home page
VACCINE AND IMMUNIZATION RESOURCES *(CID 36 355 2003)*		
American Academy of Pediatrics		www cispimmunize org
CDC National Immunization Program		www cdc gov/nip
National Network for Immunization Information		www immunizationinfo org

TABLE 22: ANTI-INFECTIVE DRUG-DRUG INTERACTIONS

Significance/Certainty: ± = theory/anecdotal; + = of probable importance; ++ = of definite importance

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	SIGNIFICANCE/ CERTAINTY
Amantadine (Symmetrel)	Alcohol	↑ CNS effects	+
	Anticholinergic and anti-Parkinson agents (ex Artane, scopolamine)	↑ effect of B dry mouth ataxia, blurred vision, slurred speech, toxic psychosis	+
	Trimethoprim	↑ levels of A & B	+
	Digoxin	↑ levels of B	±
Aminoglycosides—parenteral (amikacin gentamicin kanamycin netilmicin sisomicin streptomycin tobramycin) *NOTE Capreomycin is an aminoglycoside used as alternative drug to treat mycobacterial infections*	Amphotericin B	↑ nephrotoxicity	++
	Cis platinum (Platinol)	↑ nephro & ototoxicity	+
	Cyclosporine	↑ nephrotoxicity	+
	Neuromuscular blocking agents	↑ apnea or respiratory paralysis	+
	Loop diuretics (e g furosemide)	↑ ototoxicity	++
	NSAIDs	↑ nephrotoxicity	+
	Non-polarizing muscle relaxants	↑ apnea	+
	Radiographic contrast	↑ nephrotoxicity	+
	Vancomycin	↑ nephrotoxicity	+
Aminoglycosides—oral (kanamycin neomycin)	Oral anticoagulants (dicumarol, phenindione, warfarin)	↑ prothrombin time	+
Amphotericin B and ampho B lipid formulations	Antineoplastic drugs	↑ nephrotoxicity risk	+
	Digitalis	↑ toxicity of B if K^+ ↓	+
	Nephrotoxic drugs aminoglycosides cidofovir cyclosporine foscarnet pentamidine	↑ nephrotoxicity of A	++
Ampicillin, amoxicillin	Allopurinol	↑ frequency of rash	++
Ampranavir and fosampranavir	Antiretrovirals—*see Table 22B & C*		
	Contraceptives, oral	↓ levels of A, use other contraception	++
	Lovastatin/simvastatin	↑ **levels of B—avoid**	++
	Methadone	↓ levels of A & B	++
	Rifabutin	↑ levels of B (↓ dose by 50–75%)	++
	Rifampin	↓ **levels of A—avoid**	++
Atazanavir	*See protease inhibitors and Table 22B & C*		
Atovaquone	Rifampin (perhaps rifabutin)	↓ serum levels of A, ↑ levels of B	+
	Metoclopramide	↓ levels of A	+
	Tetracycline	↓ levels of A	++

Azole Antifungal Agents[1] [***Flu*** = fluconazole ***Itr*** = itraconazole ***Ket*** = ketoconazole ***Vor*** = voriconazole + = occurs ***blank space*** = either studied & no interaction OR no data found (may be in pharm co databases)]

Flu	Itr	Ket	Vor		
+	+			Amitriptyline	↑ levels of B	+
+	+	+	+	Calcium channel blockers	↑ levels of B	++
	+		+	Carbamazepine (vori contraindicated)	↓ levels of A	++
+	+	+	+	Cyclosporine	↑ levels of B ↑ risk of nephrotoxicity	+
	+	+		Didanosine	↓ absorption of A	+
	+	+		H_2 blockers antacids sucralfate	↓ absorption of A	+
+	+	+	+	Hydantoins (phenytoin, Dilantin)	↑ levels of B, ↓ levels of A	++
	+	+		Isoniazid	↓ levels of A	+
	+		+	Lovastatin/simvastatin	Rhabdomyolysis reported, ↑ levels of B	++
+	+	+	+	Midazolam/triazolam po	↑ levels of B	++
+	+	+	+	Oral anticoagulants	↑ effect of B	++
+	+		+	Oral hypoglycemics	↑ levels of B	++
			+	Pimozide	↑ levels of B	++
	+	+	?	Protease inhibitors	↑ levels of B	++
	+	+	+	Proton pump inhibitors	↓ absorption of A ↑ levels of B	++
+	+	+	+	Rifampin/rifabutin (vori contraindicated)	↑ levels of B, ↓ serum levels of A	++
			+	Sirolimus (vori contraindicated)	↑ levels of B	++
+		+		Tacrolimus	↑ levels of B with toxicity	++
+		+		Theophyllines	↑ levels of B	+
		+		Trazodone	↑ levels of B	++
+				Zidovudine	↑ levels of B	+

Caspofungin	Cyclosporine	↑ levels of A	++
	Tacrolimus	↓ levels of B	++
	Carbamazepine, dexamethasone, efavirenz, nelfinavir, nevirapine, phenytoin, rifamycin	↓ levels of A, ↑ dose of caspofungin to 70 mg/d	++
Cephalosporins with methyltetrathiozole-thiol side-chain	Oral anticoagulants (dicumarol warfarin) heparin thrombolytic agents platelet aggregation inhibitors	↑ effects of B bleeding	+
Chloramphenicol	Hydantoins	↑ toxicity of B, nystagmus, ataxia	++
	Iron salts Vitamin B12	↓ response to B	++
	Protease inhibitors—HIV	↑ levels of A & B	++

[1] Major interactions given unusual or minor interactions manifest as toxicity of non-azole drug due to ↑ serum levels Caffeine (Flu) digoxin (Itr) felodipine (Itr) fluoxetine (Itr) indinavir (Ket), lovastatin/simvastatin quinidine (Ket) tricyclics (Flu) vincristine (Itr) and ↓ effectiveness of oral contraceptives

TABLE 22 (2)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	SIGNIFICANCE/ CERTAINTY
Clindamycin (Cleocin)	Kaolin	↓ absorption of A	+
	Muscle relaxants, e.g., atracurium, baclofen, diazepam	↑ frequency/duration of respiratory paralysis	+
Cycloserine	Ethanol	↑ frequency of seizures	+
	INH, ethionamide	↑ frequency of drowsiness/dizziness	+
Dapsone	Didanosine	↓ absorption of A	+
	Oral contraceptives	↓ effectiveness of B	+
	Pyrimethamine	↑ in marrow toxicity	+
	Rifampin/Rifabutin	↓ serum levels of A	+
	Trimethoprim	↑ levels of A & B (methemoglobinemia)	+
	Zidovudine	May ↑ marrow toxicity	+
Delavirdine (Rescriptor)	*See non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22C*		
Didanosine (ddI) (Videx)	Cisplatin, dapsone, INH, metronidazole, nitrofurantoin, stavudine, vincristine, zalcitabine	↑ risk of peripheral neuropathy	+
	Ethanol lamivudine pentamidine	↑ risk of pancreatitis	+
	Fluoroquinolones	↓ absorption 2° to chelation	+
	Drugs that need low pH for absorption: dapsone indinavir, itra/ketoconazole pyrimethamine rifampin trimethoprim	↓ absorption	+
	Methadone	↓ levels of A	++
	Ribavirin	↑ levels ddI metabolite– **avoid**	++
	Tenofovir	↑ levels of A **(reduce dose of A)**	++
Doxycycline	Aluminum bismuth iron, Mg^{++}	↓ absorption of A	+
	Barbiturates, hydantoins	↓ serum t/2 of A	+
	Carbamazepine (Tegretol)	↓ serum t/2 of A	+
	Digoxin	↑ serum levels of B	+
	Warfarin	↑ activity of B	++
Efavirenz (Sustiva)	*See non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22C*		
Ertapenem (Invanz)	Probenecid	↑ levels of A	++
Ethambutol (Myambutol)	Aluminum salts (includes didanosine buffer)	↓ absorption of A & B	+

Fluoroquinolones (***Cipro*** = ciprofloxacin ***Gati*** = gatifloxacin ***Gemi*** = gemifloxacin ***Levo*** = levofloxacin ***Lome*** = lomefloxacin ***Moxi*** = moxifloxacin ***Oflox*** = ofloxacin)

Cipro	Gati[1]	Gemi[1]	Levo	Lome	Moxi[1]	Oflox	***NOTE: Blank space*** = *either studied and no interaction OR no data found (pharm co may have data)*		
	+		+		+		**Antiarrhythmics (procainamide, amiodarone)**	↑ Q-T interval (torsade)	++
+	+		+	+	+	+	Insulin, oral hypoglycemics	↑ & ↓ blood sugar	++
+							Caffeine	↑ levels of B	+
+				+		+	Cimetidine	↑ levels of A	+
+				+		+	**Cyclosporine**	↑ levels of B	±
+	+		+	+	+	+	Didanosine	↓ absorption of A	++
+	+	+	+	+	+	+	**Cations: Al^{+++}, Ca^{++}[1], Fe^{++}, Mg^{++}, Zn^{++} (antacids, vitamins, dairy products), citrate/citric acid**	↓ absorption of A (some variability between drugs)	++
+							Foscarnet	↑ risk of seizures	+
+							Methadone	↑ levels of B	++
+			+	+		+	**NSAIDs**	↑ risk CNS stimulation/seizures	++
+							Phenytoin	↑ or ↓ levels of B	+
+		+		+		+	Probenecid	↓ renal clearance of A	+
+	+	+	+	+		+	Sucralfate	↓ absorption of A	++
+							Theophylline	↑ levels of B	++
+			+	+		+	Warfarin	↑ prothrombin time	+

Foscarnet (Foscavir)	Ciprofloxacin	↑ risk of seizures	+
	Nephrotoxic drugs aminoglycosides, ampho B, cis-platinum, cyclosporine	↑ risk of nephrotoxicity	+
	Pentamidine IV	↑ risk of severe hypocalcemia	++
Ganciclovir (Cytovene)	Imipenem	↑ risk of seizures reported	+
	Probenecid	↑ levels of A	+
	Zidovudine	↓ levels of A, ↑ levels of B	+
Gentamicin	*See Aminoglycosides—parenteral*		
Halofantrine	Mefloquine	Additive effect prolong Q-T interval	**++ (avoid)**
Indinavir	*See protease inhibitors and Table 22B & C*		
Isoniazid	**Alcohol, rifampin**	**↑ risk of hepatic injury**	++
	Aluminum salts	↓ absorption (take fasting)	++
	Carbamazepine phenytoin	↑ levels of B with nausea, vomiting, nystagmus, ataxia	++
	Itraconazole ketoconazole	↓ levels of B	+
	Oral hypoglycemics	↓ effects of B	+
Lamivudine	Zalcitabine	**Mutual interference—do not combine**	++

[1] Neither Gatl Gemi nor Moxi interacts with Ca^{++}

TABLE 22 (3)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	SIGNIFICANCE/ CERTAINTY
Linezolid (Zyvox)	Adrenergic agents	Risk of hypertension	++
	Aged fermented pickled or smoked foods — ↑ tyramine	Risk of hypertension	+
	Serotonergic drugs (SSRIs)	Risk of serotonin syndrome	+
Lopinavir	*See protease inhibitors*		

Macrolides *[**Ery** = erythromycin **Azi** = azithromycin **Clr** = clarithromycin **Dir** = dirithromycin + = occurs **blank** = **speca** either studied and no interaction OR no data (pharm co may have data)]*

Ery	Dir	Azi	Clr			
+	+		+	Carbamazepine	↑ serum levels of B, nystagmus, nausea, vomiting, ataxia	++ **(avoid with erythro)**
+			+	Cimetidine **ritonavir**	↑ levels of B	+
+				Clozapine	↑ serum levels of B, CNS toxicity	+
+				Corticosteroids	↑ effects of B	+
+	+	+	+	Cyclosporine	↑ serum levels of B with toxicity	+
+	+	+	+	Digoxin digitoxin	↑ serum levels of B (10% of cases)	+
			+	Efavirenz	↓ levels of A	++
+	+		+	Ergot alkaloids	↑ levels of B	++
+	+		+	Lovastatin/simvastatin	↑ levels of B, rhabdomyolysis	++
+				Midazolam triazolam	↑ levels of B ↑ sedative effects	+
+	+		+	Phenytoin	↑ levels of B	+
+	+	+	+	Pimozide	↑ Q-T interval	++
+			+	Rifampin, rifabutin	↓ levels of A	+
+			+	Tacrolimus	↑ levels of B	++
+			+	Theophyllines	↑ serum levels of B with nausea, vomiting, seizures, apnea	++
+	+		+	Valproic acid	↑ levels of B	+
+	+		+	Warfarin	May ↑ prothrombin time	+
			+	Zidovudine	↓ levels of B	+
Mefloquine				ß-adrenergic blockers, calcium channel blockers quinidine, quinine	↑ arrhythmias	+
				Divalproex valproic acid	↓ level of B with seizures	++
				Halofantrine	Q-T prolongation	++ **(avoid)**
Methanamine mandelate or hippurate				Acetazolamide sodium bicarbonate thiazide diuretics	↓ antibacterial effect 2° to ↑ urine pH	++
Metronidazole				**Alcohol**	Disulfiram-like reaction	+
				Cyclosporin	↑ levels of B	++
				Disulfiram (Antabuse)	Acute toxic psychosis	+
				Lithium	↑ levels of B	++
				Oral anticoagulants	↑ anticoagulant effect	++
				Phenobarbital hydantoins	↑ levels of B	++
Nelfinavir	*See protease inhibitors and Table 22B & C*					
Nevirepine (Viramune)	*See non-nucleoside reverse transcriptase inhibitors (NNRTIs) and Table 22C*					
Nitrofurantoin	Antacids	↓ absorption of A	+			

Non-nucleoside reverse transcriptase inhibitors (NNRTIs): For interactions with protease inhibitors *see Table 22C*
Dal = delavirdine **Efe** = efavirenz **Nav** = nevirapine

Dal	Efa	Nav			
			Co-administration contraindicated:		
+			Anticonvulsants carbamazepine, phenobarbital, phenytoin		++
+			Antimycobacterials rifabutin rifampin		++
+			Antipsychotics pimozide		++
-	-		Benzodiazepines alprazolam midazolam triazolam		++
+	+		Ergotamine		++
-			HMG CoA inhibitors (statins) lovastatin simvastatin		++
+			St John's wort		++
			Dose change needed:		
+			Amphetamines	↑ levels of B—**caution**	++
+		+	Antiarrhythmics amiodarone, lidocaine others	↓ or ↑ levels of B—**caution**	++
+	+	+	Anticonvulsants carbamazepine, phenobarbital, phenytoin	↓ levels of A and/or B	++
	±	+	Antifungals itraconazole ketoconazole	Potential ↓ levels of B	+
+			Antipsychotics pimozide		++
-		+	Antirejection drugs cyclosporine rapamycin sirolimus tacrolimus	↑ levels of B	++
		+	Benzodiazepines *as above*	↑ levels of B	++
-		+	Calcium channel blockers	↑ levels of B	++
+		+	Clarithromycin	↑ levels of B metabolite	++
-		+	Cyclosporine	↑ levels of B	++
+			Dexamethasone	↓ levels of A	++
+	+	+	Sildenafil vardenafil tadalafil	↑ levels of B	++
+		+	Fentanyl methadone	↑ levels of B	++
+			Gastric acid suppression antacids H 2 blockers proton pump inhibitors	↓ levels of A	++
+			HMG-CoA inhibitors (statins)		
	+	+	Methadone	↓ levels of B	++

TABLE 22 (4)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	SIGNIFICANCE/ CERTAINTY
Non-nucleoside reverse transcriptase inhibitors (NNRTIs) *(continued)* For interactions with protease inhibitors *see Table 22B* **Del** = delavirdine **Efa** = efavirenz **Nev** = nevirapine			
Del | **Efa** | **Nev**	**Co-administration contraindicated:**		
+	Oral contraceptives	↑ or ↓ levels of B	++
+	Protease inhibitors—*see Table 22C*		
+	Rifabutin, rifampin	↑ or ↓ levels of rifabutin, ↓ levels of A—**caution**	++
+	St. John's wort	↓ levels of B	
+	Warfarin	↑ levels of B	++
Pentamidine IV	Amphotericin B	↑ risk of nephrotoxicity	+
	Foscarnet	↑ risk of hypocalcemia	+
	Pancreatitis-associated drugs e.g. alcohol valproic acid	↑ risk of pancreatitis	+
Piperacillin	Cefoxitin	Antagonism vs pseudomonas	++
Primaquine	Chloroquine dapsone INH probenecid quinine sulfonamides TMP/SMX others	↑ risk of hemolysis in G6PD-deficient patients	++

Protease inhibitors—Anti-HIV Drugs (***Ampren*** = *amprenavir & fosamprenavir* ***Atazan*** = *atazanavir* ***Indin*** = *indinavir* ***Lopin*** = *lopinavir* ***Nelfin*** = *nelfinavir* ***Riton*** = *ritonavir* ***Saquin*** = *saquinavir)* For interactions with antiretrovirals *see Table 22B & C*

Only a partial list—check package insert

Also see http://aidsinfo.nih.gov

Ampren	Atazan	Indin	Loprin	Nelfin	Riton	Saquin	
							Analgesics
					+		1. Alfentanil, fentanyl, hydrocodone, tramadol — ↑ levels of B — +
	·		+		+		2. Codeine hydromorphone morphine methadone — ↓ levels of B — +
+	+	+	+	+	+	+	**Anti-arrhythmics: amiodarone, lidocaine, mexiletine, flecainide** — ↑ levels of B — +
+		+	+	+	+	+	**Anticonvulsants: carbamazepine, clonazepam, phenytoin, phenobarbital** — ↓ levels of A ↑ levels of B — ++
+	+	+			+		Antidepressants, all tricyclic — ↑ levels of B — +
	+				+		Antidepressants all other — ↑ levels of B — +
					+		**Antihistamine** Loratadine — ↑ levels of B — ++
			+				Atovaquone — ↓ levels of B — +
+	+	+	+	+	+		**Benzodiazepines, e.g., diazepam** — ↑ **levels of B—do not use** — ++
					+		Beta blockers Metoprolol pindolol propranolol timolol — ↑ levels of B — +
+	+	+	+	+	+	+	Calcium channel blockers (all) — ↑ levels of B — ++
	+				+	+	Clarithromycin erythromycin — ↑ levels of B if renal impairment — +
	+		+	+	+		**Contraceptives, oral** — ↓ **levels of B** — ++
+			+		+	+	Corticosteroids prednisone, dexamethasone — ↓ levels of A ↑ levels of B — +
+	+	+	+	+	+	+	Cyclosporine — ↑ levels of B, monitor levels — +
+	+	+	+	+	+	+	Ergot derivatives — ↑ **levels of B—do not use** — ++
+		+		+	+	+	Erythromycin, clarithromycin — ↑ levels of A & B — +
		+		+		+	Grapefruit juice (>200 ml/day) — ↓ indinavir & ↑ saquinavir levels — ++
+	+	+	+	+	+	+	H2 receptor antagonists — ↓ levels of A — ++
+	+	+	+	+	+	+	HMG CoA reductase inhibitors (statins) lovastatin simvastatin — ↑ **levels of B—do not use** — ++
	+						Irinotecan — ↑ **levels of B—do not use** — ++
+		+	+	+		+	Ketoconazole itraconazole ? vori — ↑ levels of A ↑ levels of B — +
+			+		+		Metronidazole — Poss. disulfiram reaction, alcohol — +
+	+	+	+	+	+	+	Pimozide — ↑ **levels of B—do not use** — ++
+	+	+	+	+	+	+	Proton pump inhibitors — ↓ levels of A — ++
+	+	+	+	+	+	+	Rifampin rifabutin — ↓ levels of A ↑ levels of B — ++ **(avoid)**
+	+	+	+	+	+	+	Sildenafil (Viagra) — Varies, some ↑ & some ↓ levels of B — ++
+	+	+	+	+	+	+	**St. John's wort** — ↓ **levels of A—do not use** — ++
	+						Tenofovir — ↓ levels of B—add ritonavir — ++
		+	+		+		Theophylline — ↓ levels of B — +
+	+		+		+		Warfarin — ↑ levels of B — +
Pyrazinamide							INH rifampin — May ↑ risk of hepatotoxicity — ±
Pyrimethamine							Lorazepam — ↑ risk of hepatotoxicity — +
							Sulfonamides TMP/SMX — ↑ risk of marrow suppression — +
							Zidovudine — ↑ risk of marrow suppression — +
Quinine							Digoxin — ↑ digoxin levels ↑ toxicity — ++
							Mefloquine — ↑ arrhythmias — +
							Oral anticoagulants — ↑ prothrombin time — ++

TABLE 22 (5)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	SIGNIFICANCE/ CERTAINTY
Quinupristin/ dalfopristin (Synercid)	Anti-HIV drugs: NNRTIs & PIs	↑ levels of B	++
	Antineoplastic: vincristine docetaxel paclitaxel	↑ levels of B	++
	Calcium channel blockers	↑ levels of B	++
	Carbamazepine	↑ levels of B	++
	Cyclosporine, tacrolimus	↑ levels of B	++
	Lidocaine	↑ levels of B	++
	Methylprednisolone	↑ levels of B	++
	Midazolam diazepam	↑ levels of B	++
	Statins	↑ levels of B	++
Ribavirin	Didanosine	↑ levels of B → toxicity—**avoid**	++
	Stavudine	↓ levels of B	++
	Zidovudine	↓ levels of B	++
Rifamycins (rifampin rifabutin) *See footnote for less severe or less common interactions*[1] Ref *ArIM 162 985 2002*	Al OH, ketoconazole, PZA	↓ levels of A	+
	Atovaquone	↑ levels of A ↓ levels of B	+
	Beta adrenergic blockers (metoprolol, propranolol)	↓ effect of B	+
	Clarithromycin	↑ levels of A ↓ levels of B	++
	Corticosteroids	↑ replacement requirement of B	++
	Cyclosporine	↓ effect of B	++
	Delavirdine	↑ **levels of A, ↓ levels of B—avoid**	++
	Digoxin	↓ levels of B	++
	Disopyramide	↓ levels of B	++
	Fluconazole	↑ levels of A[1]	+
	Amprenavir, indinavir, nelfinavir, ritonavir	↑ levels of A (↓ dose of A), ↓ levels of B	++
	INH	Converts INH to toxic hydrazine	++
	Itraconazole[2], ketoconazole	↓ levels of B, ↑ levels of A[2]	++
	Methadone	↓ serum levels (withdrawal)	+
	Nevirapine	↓ **levels of B—avoid**	++
	Oral anticoagulants	Suboptimal anticoagulation	++
	Oral contraceptives	↓ effectiveness, spotting, pregnancy	+
	Phenytoin	↓ levels of B	+
	Protease inhibitors	↑ **levels of A, ↓ levels of B—CAUTION**	++
	Quinidine	↓ effect of B	+
	Sulfonylureas	↓ hypoglycemic effect	+
	Tacrolimus	↓ levels of B	++
	Theophylline	↓ levels of B	+
	TMP/SMX	↑ levels of A	+
	Tocainide	↓ effect of B	+
Rimantadine	*See Amantadine*		
Ritonavir	*See protease inhibitors and Table 22B & C*		
Saquinavir	*See protease inhibitors and Table 22B & C*		
Stavudine	Dapsone, INH	May ↑ risk of peripheral neuropathy	±
	Ribavirin	↓ levels of A—**avoid**	++
	Zidovudine	Mutual interference—do not combine	++
Sulfonamides	Cyclosporine	↓ cyclosporine levels	+
	Methotrexate	↑ antifolate activity	+
	Oral anticoagulants	↑ prothrombin time bleeding	+
	Phenobarbital rifampin	↓ levels of A	+
	Phenytoin	↑ levels of B nystagmus ataxia	+
	Sulfonylureas	↑ hypoglycemic effect	+
Telithromycin (Ketek)	Carbamazine	↓ levels of A	++
	Digoxin	↑ levels of B—do digoxin levels	++
	Ergot alkaloids	↑ **levels of B—avoid**	++
	Itraconazole, ketoconazole	↑ levels of A, no dose change	+
	Metoprolol	↑ levels of B	++
	Midazolam	↑ levels of B	++
	Phenobarb phenytoin	↓ levels of A	++
	Pimozide	↑ **levels of B; QT prolongation—AVOID**	++
	Rifampin	↓ **levels of A—avoid**	++
	Simvastatin & other "statins"	↑ levels of B	++
	Sotalol	↓ levels of B	++
Tenofovir	Atazanavir	↓ levels of B—add ritonavir	++
	Didanosine (ddI)	↑ **levels of B (reduce dose)**	++
Terbinafine	Cimetidine	↑ levels of A	+
	Phenobarbital rifampin	↓ levels of A	+

[1] **The following is a partial list of drugs with rifampin-induced ↑ metabolism and hence lower than anticipated serum levels: ACE inhibitors, dapsone, diazepam, digoxin, diltiazem, doxycycline, fluconazole, fluvastatin, haloperidol, nifedipine, progestins, triazolam, tricyclics, voriconazole, zidovudine**

[2] Up to 4 weeks may be required after RIF discontinued to achieve detectable serum itra levels ↑ levels associated with uveitis or polymyolysis

TABLE 22 (6)

ANTI-INFECTIVE AGENT (A)	OTHER DRUG (B)	EFFECT	SIGNIFICANCE/ CERTAINTY
Tetracyclines	*See Doxycycline plus*		
	Atovaquone	↓ levels of B	+
	Digoxin	↑ toxicity of B (may persist several months—up to 10% pts)	++
	Methoxyflurane	↑ toxicity, polyuria, renal failure	+
	Sucralfate	↓ absorption of A (separate by ≥2 hrs)	+
Thiabendazole	Theophyllines	↑ serum theophylline, nausea	+
Tinidazole (Tindamax)	*See Metronidazole—similar entity, expect similar interactions*		
Tobramycin	*See Aminoglycosides*		
Trimethoprim	Amantadine dapsone digoxin methotrexate procainamide zidovudine	↑ serum levels of B	++
	Potassium-sparing diuretics	↑ serum K^+	++
	Thiazide diuretics	↓ serum Na^+	+
Trimethoprim/Sulfamethoxazole	Azathioprine	Reports of leukopenia	+
	Cyclosporine	↓ levels of B ↑ serum creatinine	+
	Loperamide	↑ levels of B	+
	Methotrexate	Enhanced marrow suppression	++
	Oral contraceptives, pimozide, and 6-mercaptopurine	↓ effect of B	+
	Phenytoin	↑ levels of B	+
	Rifampin	↑ levels of B	+
	Warfarin	↑ activity of B	+
Vancomycin	Aminoglycosides	↑ frequency of nephrotoxicity	++
Zalcitabine (ddC) (HIVID)	Valproic acid pentamidine (IV) alcohol lamivudine	↑ pancreatitis risk	+
	Cisplatin, INH, metronidazole, vincristine, nitrofurantoin, d4T, dapsone	↑ risk of peripheral neuropathy	+
Zidovudine (ZDV) (Retrovir)	Atovaquone fluconazole metha done	↑ levels of A	+
	Clarithromycin	↓ levels of A	±
	Indomethacin	↑ levels of ZDV toxic metabolite	+
	Nelfinavir	↓ levels of A	++
	Probenecid TMP/SMX	↑ levels of A	+
	Ribavirin	↓ levels of A—avoid	++
	Rifampin/rifabutin	↓ levels of A	++

TABLE 22B. DRUG-DRUG INTERACTIONS BETWEEN PROTEASE INHIBITORS
(Adapted from Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults & Adolescents; see *www.aidsinfo.nih.gov*)

NAME (Abbreviation, Trade Name)	Amprenavir (APV Agenerase)	Atazanavir (ATV Reyataz)	Fosamprenavir (FOS APV Lexiva)	Indinavir (IDV Crixivan)	Lopinavir/Ritonavir (LP/R Kaletra)	Nelfinavir (NFV Viracept)	Ritonavir (RTV Norvir)	Saquinavir (SQV Fortovase/Invirase)
Amprenavir (APV Agenerase)				Levels APV AUC[1] ↑ 33% Doses standard	Dose APV 750 mg bid, LP/R either standard or ↑ to 533/133 mg bid	Levels APV AUC[1] ↑ 1 5X Dose Inadequate data	Dose 600/100 mg APV/RTV bid or 1200/200 mg qd	Levels APV AUC[1] ↓ 32% Dose Insufficient data
Atazanavir (ATV Reyataz)				**Do not co-administer, risk of additive ↑ in indirect bilirubin**	RTV 100 mg ↑ ATV AUC[1] 238%		ATV/RTV 300/100 mg qd	SQV (Invirase) 1200 mg qd + ATV 400 mg qd
Fosamprenavir (FQS-APV, Lexiva)					↓ serum conc both drugs, **do not co-administer**		200 mg RTV qd + FQS-APV 1400 mg qd	Insufficient data
Indinavir (IDV Crixivan)	Levels APV AUC[1] ↑ 33% Doses not established	**Do not co-administer; risk of additive ↑ in bilirubin**			IDV AUC[1] ↑ IDV dose 600 mg bid	↑ IDV & NFV levels Dose IDV 1200 mg bid NFV 1250 mg bid	Dose IDV/RTV bid as 800/100 or 800/200 mg	SQV levels ↑ 4–7 fold Dose Insufficient data
Lopinavir/Ritonavir (LP/R Kaletra)	Dose APV 750 mg bid LP/R either standard or ↑ to 533/133 mg bid	RTV 100 mg ↑ ATV AUC[1] 238%	↓ serum conc both drugs **do not co-administer**	IDV AUC[1] ↑ IDV dose 600 mg bid		Dose LP/R 533/133 mg bid, NFV 1000 mg bid	LP is co-formulated with RTV	SQV levels ↑ Dose SQV (Fortovase) 1000 mg bid LP/R standard
Nelfinavir (NFV Viracept)	Levels APV AUC[1] ↑ 1 5X Dose Inade quate data			↑ IDV & NFV levels Dose IDV 1200 mg bid NFV 1250 mg bid	LP levels ↓ NFV levels ↑ Dose No data		Dose RTV 400 mg bid + NFV 500–750 mg bid	Dose NFV standard Fortovase 800 mg tid or 1200 mg bid
Ritonavir (RTV, Norvir)	Dose 600/100 mg APV/RTV bid or 1200/200 mg qd	ATV/RTV 300/100 mg qd	200 mg RTV qd + FOS-APV 1400 mg qd	Dose IDV/RTV bid as 800/100 or 800/200 mg	LP is co-formulated with RTV	Dose RTV 400 mg bid + NFV 500–750 mg bid		Dose 1000 SQV softgel/ 100 RTV bid or 400/400 mg bid
Saquinavir (SQV Fortovase/ Invirase)	Levels APV AUC[1] ↓ 32% Dose Insuffi cient data	SQV (Invirase) 1600 mg qd + ATV 300 mg qd + RTV 100 mg qd	SQV (Invirase) 1000 mg bid + RTV 100–200 mg bid + FOS-APV 700 mg bid	SQV levels ↑ 4–7 fold Dose Insufficient data	SQV levels ↑ Dose SQV (Fortovase) 1000 mg bid LP/R standard	Dose NFV standard Fortovase 800 mg tid or 1200 mg bid	Dose 1000 SQV softgel/100 RTV bid or 400/400 mg bid	

TABLE 22C: DRUG-DRUG INTERACTIONS BETWEEN NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs) AND PROTEASE INHIBITORS.
(Adapted from Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults & Adolescents; see *www.aidsinfo.nih.gov*)

NAME (Abbreviation, Trade Name)	Amprenevir (APV Agenerase)	Atazanavir (ATV Reyataz)	Fosamprenavir (FOS-APV Lexiva)	Indinavir (IDV Crixivan)	Lopinavir/Ritonavir (LP/R Kaletra)	Nelfinavir (NFV Viracept)	Ritonavir (RTV Norvir)	Saquinavir—softgel (SQV Fortovase)
Delavirdine (DLV Rescriptor)	APV AUC[1] ↑ 130%, DLV AUC[1] ↓ 61% Do not co-administer	No data	**Co-administration not recommended**	IDV levels ↑ 40% Dose IDV 600 mg q8h, DLV standard	Expect LP levels to ↑ No dose data	NFV levels ↑ 2X, DLV levels ↓ 50% Dose No data	Levels of RTV ↑ 70% Dose DLV standard, RTV no data	SQV levels ↑ 5X Dose SQV 800 mg tid, DLV standard
Efavirenz (EFZ Sustiva)	APV AUC[1] ↓ 36% Dose EFZ standard—add RTV 200 mg to standard APV	ATV AUC[1] ↓ 74% Dose EFZ standard ATA/RTV 300/100 mg qd with food	FOS APV levels ↓ Dose EFZ standard FOS-APV 1400 mg + RTV 300 mg qd or 700 mg FOS APV + 100 mg RTV bid	Levels IDV ↓ 31% Dose IDV 1000 mg q8h EFV standard	Level of LP ↓ 40% Dose LP/R 533/133 mg bid EFZ standard	Standard doses	Standard doses	Level SQV ↓ 62% Dose SQV softgel 400 mg + RTV 400 mg bid
Nevirapine (NVP, Viramune)	No data	No data	No data	IDV levels ↓ 28% Dose IDV 1000 mg q8h or combine with RTV, NVP standard	LP levels ↓ 53% Dose LP/R 533/133 mg bid, NVP standard	Standard doses	Standard doses	Dose SQV softgel + RTV 400/400 mg both bid

[1] AUC = area under the curve

TABLE 23: LIST OF GENERIC AND COMMON TRADE NAMES

GENERIC NAME: TRADE NAMES	GENERIC NAME: TRADE NAMES	GENERIC NAME: TRADE NAMES
Abacavir Ziagen	Drotrecogin alfa Xigris	Nitazoxanide Alinia
Acyclovir Zovirax	Efavirenz Sustiva	Nitrofurantoin Macrobid Macrodantin
Adefovir Hepsera	Emtricitabine Emtriva	Nystatin Mycostatin
Albendazole Albenza	Emtricitabine + tenofovir Truvada	Ofloxacin Floxin
Amantadine Symmetrel	Enfuvirtide (T-20) Fuzeon	Oseltamivir Tamiflu
Amikacin Amikin	Ertapenem Invanz	Oxacillin Prostaphlin
Amoxicillin Amoxil Polymox	Erythromycin(s) Ilotycin	Palivizumab Synagis
Amox /clav Augmentin, Augmentin ES-600 Augmentin XR	*Ethyl succinate* Pediamycin *Glucoheptonate* Erythrocin *Estolate* Ilosone	Paromomycin Humatin
Amphotericin B Fungizone	Erythro/sulfisoxazole Pediazole	Pentamidine NebuPent Pentam 300
Ampho B-liposomal AmBisome	Ethambutol Myambutol	Piperacillin Pipracil
Ampho B-cholesteryl complex Amphotec	Ethionamide Trecator	Piperacillin/tazobactam Zosyn
Ampho B-lipid complex Abelcet	Famciclovir Famvir	Piperazine Antepar
Ampicillin Omnipen Polycillin	Fluconazole Diflucan	Podophyllotoxin Condylox
Ampicillin/sulbactam Unasyn	Flucytosine Ancobon	Praziquantel Biltricide
Amprenavir Agenerase	Fosamprenavir Lexiva	Primaquine Primachine
Atazanavir Reyataz	Foscarnet Foscavir	Proguanil Paludrine
Atovaquone Mepron	Fosfomycin Monurol	Pyrantel pamoate Antiminth
Atovaquone + proguanil Malarone	Furazolidone Furoxone	Pyrimethamine Daraprim
Azithromycin Zithromax	Ganciclovir Cytovene	Pyrimethamine/sulfadoxine Fansidar
Aztreonam Azactam	Gatifloxacin Tequin	Quinupristin/dalfopristin Synercid
Caspofungin Cancidas	Gemifloxacin Factive	Ribavirin Virazole Rebetol
Cefaclor Ceclor Ceclor CD	Gentamicin Garamycin	Rifabutin Mycobutin
Cefadroxil Duricef	Griseofulvin Fulvicin	Rifampin Rifadin Rimactane
Cefazolin Ancef Kefzol	Halofantrine Halfan	Rifapentine Priftin
Cefdinir Omnicef	Idoxuridine Dendrid Stoxil	Rifaximin Xifaxan
Cefditoren pivoxil Spectracef	INH + RIF Rifamate	Rimantadine Flumadine
Cefepime Maxipime	INH + RIF + PZA Rifater	Ritonavir Norvir
Cefixime[NUS] Suprax	Interferon alfa Roferon-A Intron A	Saquinavir Invirase Fortovase
Cefotaxime Claforan	Interferon pegylated PEG-Intron Pegasys	Spectinomycin Trobicin
Cefotetan Cefotan	Interferon + ribavirin Rebetron	Stavudine Zerit
Cefoxitin Mefoxin	Imipenem + cilastatin Primaxin	Stibogluconate Pentostam
Cefpodoxime proxetil Vantin	Imiquimod Aldara	Silver sulfadiazine Silvadene
Cefprozil Cefzil	Indinavir Crixivan	Sulfamethoxazole Ganfanol
Ceftazidime Fortaz Tazicef, Tazidime	Itraconazole Sporanox	Sulfasalazine Azulfidine
Ceftibuten Cedax	Iodoquinol Yodoxin	Sulfisoxazole Gantrisin
Ceftizoxime Cefizox	Ivermectin Stromectol	Telithromycin Ketek
Ceftriaxone Rocephin	Kanamycin Kantrex	Tenofovir Viread
Cefuroxime Zinacef Keturox Ceftin	Ketoconazole Nizoral	Terbinafine Lamisil
Cephalexin Keflex	Lamivudine Epivir Epivir HBV	Thalidomide Thalomid
Cephradine Anspor Velosef	Lamivudine + abacavir Epzicom	Thiabendazole Mintezol
Chloroquine Aralen	Levofloxacin Levaquin	Ticarcillin Ticar
Cidofovir Vistide	Linezolid Zyvox	Tinidazole Tindamax
Ciprofloxacin Cipro Cipro XR	Lomefloxacin Maxaquin	Tipranavir Texega
Clarithromycin Biaxin Biaxin XL	Lopinavir/ritonavir Kaletra	Tobramycin Nebcin
Clindamycin Cleocin	Loracarbef Lorabid	Tretinoin Retin A
Clofazimine Lamprene	Mafenide Sulfamylon	Trifluridine Viroptic
Clotrimazole Lotrimin Mycelex	Mebendazole Vermox	Trimethoprim Proloprim Trimpex
Cloxacillin Tegopen	Mefloquine Lariam	Trimethoprim/sulfamethoxazole Bactrim Septra
Colistimethate Coly-Mycin M	Meropenem Merrem	Valacyclovir Valtrex
Cycloserine Seromycin	Mesalamine Asacol Pentasa	Valganciclovir Valcyte
Daptomycin Cubicin	Methenamine Hiprex Mandelamine	Vancomycin Vancocin
Delavirdine Rescriptor	Metronidazole Flagyl	Voriconazole Vfend
Dicloxacillin Dynapen	Minocycline Minocin	Zalcitabine HIVID
Didanosine Videx	Moxifloxacin Avelox	Zanamivir Relenza
Diethylcarbamazine Hetrazan	Mupirocin Bactroban	Zidovudine (ZDV) Retrovir
Diloxanide furoate Furamide	Nafcillin Unipen	Zidovudine + 3TC Combivir
Dirithromycin Dynabac	Nelfinavir Viracept	Zidovudine + 3TC + abacavir Trizivir
Doxycycline Vibramycin	Nevirapine Viramune	
Cycloserine Seromycin		
Daptomycin Cubicin		

TABLE 23 (2)
LIST OF COMMON TRADE AND GENERIC NAMES

TRADE NAME: GENERIC NAME	TRADE NAME: GENERIC NAME	TRADE NAME: GENERIC NAME
Abelcet Ampho B lipid complex	Gantrisin Sulfisoxazole	Retin A Tretinoin
Agenerase Amprenavir	Garamycin Gentamicin	Retrovir Zidovudine (ZDV)
Albenza Albendazole	Halfan Halofantrine	Reyataz Atazanavir
Aldara Imiquimod	Hepsera Adefovir	Rifadin Rifampin
Alinia Nitazoxanide	Herplex Idoxuridine	Rifamate INH + RIF
AmBisome Ampho B-liposomal	Hiprex Methenamine hippurate	Rifater INH + RIF + PZA
Amikin Amikacin	HIVID Zalcitabine	Rimactane Rifampin
Amoxil Amoxicillin	Humatin Paromomycin	Rocephin Ceftriaxone
Amphotec Ampho B-cholesteryl complex	Ilosone Erythromycin estolate	Roferon-A Interferon alfa
Ancef Cefazolin	Ilotycin Erythromycin	Septra Trimethoprim/sulfa
Ancobon Flucytosine	Intron A Interferon alfa	Seromycin Cycloserine
Anspor Cephradine	Invanz Ertapenem	Silvadene Silver sulfadiazine
Antepar Piperazine	Invirase Saquinavir	Spectracef Cefditoren pivoxil
Antiminth Pyrantel pamoate	Kantrex Kanamycin	Sporanox Itraconazole
Aralen Chloroquine	Kaletra Lopinavir/ritonavir	Stoxil Idoxuridine
Asacol Mesalamine	Keflex Cephalexin	Stromectol Ivermectin
Augmentin Augmentin ES 600 Augmentin XR Amox /clav	Kefurox Cefuroxime	Sulfamylon Mafenide
	Ketek Telithromycin	Suprax Cefixime[NUS]
	Lamisil Terbinafine	Sustiva Efavirenz
Avelox Moxifloxacin	Lamprene Clofazimine	Symmetrel Amantadine
Azactam Aztreonam	Lariam Mefloquine	Synagis Palivizumab
Azulfidine Sulfasalazine	Levaquin Levofloxacin	Synercid Quinupristin/dalfopristin
Bactroban Mupirocin	Lexiva Fosamprenavir	Tamiflu Oseltamivir
Bactrim Trimethoprim/ sulfamethoxazole	Lorabid Loracarbef	Tazicef Ceftazidime
	Macrodantin Macrobid Nitrofurantoin	Tegopen Cloxacillin
Biaxin Biaxin XL Clarithromycin	Malarone Atovaquone + proguanil	Tequin Gatifloxacin
Biltricide Praziquantel	Mandelamine Methenamine mandel	Texega Tipranavir
Cancidas Caspofungin	Maxaquin Lomefloxacin	Thalomid Thalidomide
Ceclor Ceclor CD Cefaclor	Maxipime Cefepime	Ticar Ticarcillin
Cedax Ceftibuten	Mefoxin Cefoxitin	Timentin Ticarcillin clavulanic acid
Cefizox Ceftizoxime	Mepron Atovaquone	Tinactin Tolnaftate
Cefotan Cefotetan	Merrem Meropenem	Tindamax Tinidazole
Ceftin Cefuroxime axetil	Minocin Minocycline	Trecator SC Ethionamide
Cefzil Cefprozil	Minfezol Thiabendazole	Trizivir Abacavir + ZDV + 3TC
Cipro Cipro XR Ciprofloxacin & extended release	Monocid Cefonicid	Trobicin Spectinomycin
	Monurol Fosfomycin	Truvada Emtricitabine + tenofovir
Claforan Cefotaxime	Myambutol Ethambutol	Unasyn Ampicillin/sulbactam
Coly-Mycin M Colistimethate	Mycobutin Rifabutin	Unipen Nafcillin
Combivir ZDV + 3TC	Mycostatin Nystatin	Valcyte Valganciclovir
Crixivan Indinavir	Nafcil Nafcillin	Valtrex Valacyclovir
Cubicin Daptomycin	Nebcin Tobramycin	Vancocin Vancomycin
Cytovene Ganciclovir	NebuPent Pentamidine	Vantin Cefpodoxime proxetil
Daraprim Pyrimethamine	Nizoral Ketoconazole	Velosef Cephradine
Diflucan Fluconazole	Norvir Ritonavir	Vermox Mebendazole
Duricef Cefadroxil	Omnicef Cefdinir	Vfend Voriconazole
Dynapen Dicloxacillin	Omnipen Ampicillin	Vibramycin Doxycycline
Emtriva Emtricitabine	Pediamycin Erythro ethyl succinate	Videx Didanosine
Epivir Epivir-HBV Lamivudine	Pediazole Erythro ethyl succinate + sulfisoxazole	Viracept Nelfinavir
Epzicom Lamivudine + abacavir		Viramune Nevirapine
Factive Gemifloxacin	Pegasys PEG Intron Interferon pegylated	Virazole Ribavirin
Famvir Famciclovir		Viread Tenofovir
Fansidar Pyrimethamine + sulfadoxine	Pentam 300 Pentamidine	Vistide Cidofovir
	Pentasa Mesalamine	Xifaxan Rifaximin
Flagyl Metronidazole	Pipracil Piperacillin	Xigris Drotrecogin alfa
Floxin Ofloxacin	Polycillin Ampicillin	Yodoxin Iodoquinol
Flumadine Rimantadine	Polymox Amoxicillin	Zerit Stavudine
Fortaz Ceftazidime	Priftin Rifapentine	Ziagen Abacavir
Fortovase Saquinavir	Primaxin Imipenem + cilastatin	Zinacef Cefuroxime
Fulvicin Griseofulvin	Proloprim Trimethoprim	Zithromax Azithromycin
Fungizone Amphotericin B	Prostaphlin Oxacillin	Zovirax Acyclovir
Furadantin Nitrofurantoin	Rebetol Ribavirin	Zosyn Piperacillin/tazobactam
Furoxone Furazolidone	Rebetron Interferon + ribavirin	Zyvox Linezolid
Fuzeon Enfuvirtide (T-20)	Relenza Zanamivir	
Gantanol Sulfamethoxazole	Rescriptor Delavirdine	

INDEX TO MAJOR ENTITIES

PAGES *(page numbers bold if major focus)*

Bold numbers indicate major considerations. Recommendations in Table 1 not indexed; antibiotic selection often depends on modifying circumstances and alternative agents.

PAGES *(page numbers bold if major focus)*

PRICING:

	Quantity	2005 Price Each	2006 Pre-order Price Each
Pocket Ed (English & Spanish)	1-9	10.00	10.50
	10-49	9.50	10.00
	50+	9.00	9.50
Clear Vinyl Cover (English pocket ed)		1.00	1.00
PDA Installer CD	1-9	27.50	27.50
	10-19	25.00	25.00
	20+	23.75	23.75
Spiral Editions	1-9	25.00	25.00
	10-19	23.75	23.75
	20+	23.25	23.25

SHIPPING:

Shipping charges will be added to your order.

Standard Shipping Methods:

US: First Class Mail or UPS Ground
Canada: Airmail or UPS Ground
International: Airmail

Optional worldwide express shipping by FedEx

Please contact us with any shipping questions.

Selected small quantity shipping charges for U.S. orders.

Qty	*Pocket*	*Spiral*	*CD*
1	1.50	3.00	3.00
2	3.00	6.00	5.50
5	7.00	8.00	7.00
10	8.00	10.50	7.00
20	9.00	11.50	9.00
25	10.00	15.00	10.00
50	12.00	25.00	13.50

ORDERING:

Mail: Antimicrobial Therapy, Inc.
P.O. Box 70
229 Main Street
Hyde Park, VT 05655 USA

Email: info@sanfordguide.com
Fax: 802 888 2874
Phone: 802 888 2855

Web: www.sanfordguide.com (Secure online ordering)

SANFORD GUIDE 2005 ORDER FORM

2005 Pocket Editions:	**Qty**	**Price Each**	**Extension**
Antimicrobial Therapy 2005 (English)			
HIV/AIDS Therapy 2005			
Antimicrobial Therapy 2005 (Spanish)			
2005 Spiral Editions:			
Antimicrobial Therapy 2005			
HIV/AIDS Therapy 2005			
2005 PDA Editions (Installer CD):			
Antimicrobial Therapy 2005			
HIV/AIDS Therapy 2005			
2006 Pocket Editions (Preorder):			
Antimicrobial Therapy 2006 (English)			
HIV/AIDS Therapy 2006			
Antimicrobial Therapy 2006 (Spanish)			
2006 Spiral Editions:			
Antimicrobial Therapy 2006			
HIV/AIDS Therapy 2006			
2006 PDA Editions (Installer CD):			
Antimicrobial Therapy 2006			
HIV/AIDS Therapy 2006			
Clear Vinyl Cover for Pocket Ed			

Sales Tax: TX 6.25%, VT 6%, VA 5%

All orders must be prepaid.

We accept *Visa, Mastercard, American Express*.

Checks must be in U.S. Funds from a U.S. bank account.

Subtotal	
Sales Tax	
Shipping	
TOTAL	

Card Number

/

Expires

Cardholder Signature

Billing/ Shipping Address: Complete reverse side of card

Cardholder Name (print)

BILLING ADDRESS:

Name

Company

Address

Address

City, State Postal Code

Country

SHIPPING ADDRESS (if different):

Address

City, State Postal Code

Country

Tel, Fax, Email:

Tel:

Fax:

Notice: We do not share this information. Its only use is to contact you concerning your order.

Email:

RAPID REFERENCE

20503489(1)-04/05-PRI